New Orleans Medical
and
Surgical Journal

Vol. 101 JULY, 1948 No. 1

SYMPOSIUM ON BIOPSY PROCEDURE IN CANCER AND PRECANCEROUS LESIONS

BIOPSY IN OTOLARYNGOLOGY*

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Everything that can be said concerning biopsy in other fields can also be said concerning its use in otolaryngology. By the use of biopsy we come nearer to distinguishing with absolute accuracy between benign and malignant disease than with any other diagnostic aid we possess. It thus guarantees that no patient shall be submitted unnecessarily to surgery, which must always be radical, and which frequently is potentially lethal. Finally, biopsy is most useful, and the percentage of curability is highest, when it is used not to substantiate a clinically established fact but to confirm or exclude the mere suspicion that malignant disease exists.

These are generally applicable principles. There are, in addition, certain considerations particularly applicable to biopsy in otolaryngology which I shall present briefly by the question and answer method.

When should biopsy be performed in otolaryngology? The answer is categoric: Whenever the smallest doubt arises as to the nature of the tissue in a given area, particularly if the tissue is neoplastic; and whenever such symptoms as hoarseness, a persistent cough, dysphagia, or other symptoms and signs referable to the ear, nose and throat cannot be promptly and fully explained on the basis of a non-malignant disease process.

Where should biopsy be performed? The answer is, always in the hospital. The average physician does not have in his office all the necessary equipment for biopsy. If he does have the equipment, he does not have the means or the personnel to protect the patient in the event of hemorrhage or other untoward events. It should never be forgotten that bronchoscopy, esophagoscopy, and even laryngoscopy are serious procedures, employment of which while it should not be, has been attended with grave complications, some of which have terminated fatally.

What anesthesia is required? Biopsy of tissue in the ear, nose, throat, and bronchi requires only topical applications of cocaine, pontocaine, or some similar agent. It is essential that the patient be free from discomfort, but inhalation anesthesia is not necessarily desirable.

What points of technic are important? Several considerations should be borne in mind: (1) Appropriate instruments must be used, including, in addition to endoscopic equipment, snares, punch forceps and biting forceps. Dissection of the specimen is not required but electrocauterization of the area later is useful. (2) Biopsy must be done under absolutely sterile conditions and with careful hemostasis. (3) The specimen must be removed under full vision, to be certain that it is properly selected and to be certain also that important structures are not harmed by blind manipulations.

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*Read at meeting of the Orleans Parish Medical Society, November 10, 1947.

(4) Special technics are useful in special areas. If bronchoscopy, for instance, reveals apparently normal tissue throughout the field of vision, scraping (so-called scalping) of the mucosa will provide sufficient tissue for cytologic diagnosis. I have myself distinguished between tuberculosis with negative sputum, and malignancy, in at least four cases by this method. (5) Whenever the suspected tissue is small, the area should be removed in toto. It is perfectly possible in such conditions as granuloma of the vocal cords, for instance, to perform biopsy and eradicate the lesion at the same time.

How shall the specimen be preserved? The otolaryngologic specimen is always small and must be handled with particular care. It should be kept moist, in saline or some other solution, and it should be examined as promptly as possible, especially if it consists only of scrapings. Specimens which must be examined in distant laboratories should be in 5 or 10 per cent formalin solution, packed in special containers, and sent air mail special delivery.

How should a negative report be evaluated? It should not be accepted as final unless it accords with the clinical course. If suspicion still exists, the biopsy should be repeated one or more times, and such a procedure as exploratory thoracotomy is fully warranted if such a condition as carcinoma of the lung cannot otherwise be excluded.

How far should one be guided by the pathologist? If he is competent—and the otolaryngologist should deal with no other kind—his advice should be accepted absolutely. It may be a truism, but it is everlastingly true, that the more experienced the physician, the less does he need the pathologist and the more is he likely to use him. The otolaryngologist is on firm ground when he bases his therapeutic course on a competent pathologist's interpretation of an adequate specimen of tissue secured by biopsy.

BIOPSY IN GASTROINTESTINAL PRACTICE*

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The field of gastroenterology, in our opinion, encompasses those diagnostic procedures essential to the detailed study of the digestive tract extending from the crichopharyngeal portion of the esophagus to the anus. This broad inclusion may seem an encroachment to some specialists: the bronchoesophagologist may consider esophagoscopy his procedure; the surgeon may conclude peritoneoscopy is in his realm; the proctologist often considers himself diagnostician as well as operator.

The invasion of gastroenterologists into endoscopy and biopsy, however, arose from seeming reluctance on the part of the specialists mentioned to aid in rendering a conclusive biopsy diagnosis. By biopsy, of course, we are presuming the inclusion of cytologic study of material obtained by such simple measures as gastric and small bowel aspiration and paracentesis, as well as through endoscopic aids. Just how much the more recent cytologic stains add to the previous staining methods awaits evaluation.

With sincere reservation we select our cases for esophagoscopy, practice meticulous delicacy in instrumentation, but find it simpler to omit an attempt at sterile technic and hospitalization for the performance of routine esophagoscopic study. A skilled esophagoscopist with capable assistance can adopt esophagoscopy to office usage just as well as gastroscopy and proctosigmoidoscopy. Our experience in the Touro Clinic, where we are forced to esophagoscope our negro patients, since no hospital service is available to them, substantiates this statement. As a conclusive

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differential study as to the cause of dysphagia, when supplemented by biopsy, it has given unsurpassed assistance. It must be understood tha normal mucosa is not biopsied. We do not use a sharp biting biopsy forcep but prefer a blunt cupped (ball-bearing) forcep which merely picks up a piece of tissue. Biopsies should not exceed mucosal depth. We advocate placing a small piece of fibrin-foam to the biopsy site to seal it and stop bleeding. The ambulatory patient leaves after an hour's rest, which permits recovery from pontocaine anesthesia.

Hepatic needle biopsy is gaining acceptance. Tripoli and Fader introduced the procedure to New Orleans in 1941. W. D. Davis gave an excellent review of the progress in this field together with his personal observation in 128 instances at the April 14, 1947 meeting of this Society. Davis, among others, is an advocate of the Roth-Turkel needle; our preference is an elongated Vim-Silverman needle. We still adhere to the adjunctive use of peritoneoscopy to visualize the site of biopsy. With peritoneoscopy, proper preparation, use of a Vim-Silverman needle, subcostal approach and the post biopsy injection of fibrin-foam, we feel that accuracy approaches 96 per cent and the danger is minimal. Our experience with this method is illustrated by the following chart on 50 peritoneoscopic hepatic studies:

Primary Hepatoma	2
Metastatic Carcinoma	12
Melanosarcoma	1
Hemangioma	1
Suppurative Hepatitis (abscess)	1
Hemochromatosis	1
Acute Infectious Hepatitis	4
Fatty Liver	10
Chronic Hepatitis (Cirrhosis)	12
Normal Liver	6
	50

Unfortunately neither alone, nor with peritoneoscopy is the procedure adaptable to office routine. It is beyond our hope that even with improved technic and reassurance from satisfactory coagulation that it will ever be safe for ambulatory patients to be so studied. While many authors claim diagnostic valuation to extremes it is our belief that peritoneoscopy can only give accurate information on the liver, peritoneum, omentum, and on the exposed visceral surfaces easily visualized. One must recognize definite limitations for this examination.

CONCLUSION

Herewith is further support for biopsy. Gastroenterologists are firmly entrenched in a stand for biopsy diagnosis; their field lends itself well to such conclusive study.

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THE BIOPSY IN DERMATOLOGY*

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In dermatology biopsies are frequently necessary to corroborate the clinical diagnosis. It is by this procedure that skin cancer is diagnosed and that its origin, type, and degree are determined. Alerted by behavior changes in various chronic premalignant lesions, such as leukoplakia, kraurosis vulvae, chronic ulcers, and pigmented moles, we search for transitions into malignancy. Our histologic study can determine therapy and establish a prognosis.

We are careful to tell our patients why we require this study and that our full opinion in their case will be deferred until this is completed. It is not well to use the term "cancer" when we are seeking specimens, for that would be tantamount to giving a diagnosis and patients would be convinced that they had cancer no matter what the biopsy showed. It is well also to find out their tolerance to local anesthetics, whether or not they heal with unsightly keloid, and whether they are bleeders.

To obtain a proper specimen, select a margin away from infected areas. Infiltrate around and beneath but not into the selected site. In small lesions such as small epitheliomas, excise the entire lesion and thoroughly cauterize the base with the actual cautery. Thus, in some instances,

*Read before meeting of the Orleans Parish Medical Society, November 10, 1947.

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treatment may be completed at the same time the specimen is secured.

In larger lesions, select the margin and include some of the normal skin for comparative histologic study. The centers are too often infected or have undergone fibrous healing or destructive non-specific changes. In pigmented moles we do not biopsy. We excise the entire lesion. Subsequent histologic study of this specimen will show whether this excision has been complete.

If the melanotic lesion is large or if metastasis is suspected because of regional gland enlargement, the case should be handled by a surgeon. With mucocutaneous junction lesions such as those of the lip, genital, or anal regions, surgical confreres are brought into the case, as often the frozen section and extensive surgery in the operating room are life-saving. It is well to understand and follow lines of cleavage for good cosmetic results.

Place the biopsy specimen in 2 per cent formalin and send it to the pathologist. If the specimen is very small and there would be a question as to which is the upper surface, place it on a small piece of paper with any side touching the paper except the base or upper surface, and drop upside down in formalin solution. The pathologist can incorporate this paper in his paraffin block, cut sections parallel to the paper, and thus avoid tangential sections which are useless and annoying. Do not expect good information from a shaved specimen. Send a good history and clinical description with each specimen.

The danger of causing epitheliomas to spread by biopsy is not considered great if the safeguards for handling pigmented lesions and mucocutaneous lesions are followed.

OFFICE BIOPSY IN OBSTETRICS AND GYNECOLOGY*

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Gynecologic cancer is represented most conspicuously by cancer of the uterus. The purpose of this paper is diagnosis of cancer from the gynecological viewpoint and discussion particularly of the newer methods of diagnosis of uterine cancer.

Before doing this, however, it is deemed wise to make a few observations regarding cancer from a general standpoint. It is believed that the cause of cancer is intracellular rather than an extrinsic factor such as a virus, the normal cell being transformed into a gangster cell of cancer. Heredity is believed by many to play an important part in cancer. Chronic irritations are supposed to predispose to the development of carcinoma. Ovarian hormones also play a possible role in carcinogenesis. Precancerous lesions are those lesions which histologically are of borderline type and which therefore are difficult to diagnose microscopically.

Formerly surgical biopsy was the only method used to confirm diagnosis. Now, with newer methods biopsies are increasing due to earlier diagnosis of cancer even in cases in which the cervix is normal in appearance.

METHODS

The methods of detection include use of the finger, the eye, and biopsy. The following are some of the office procedures:

1) Colposcopic examination introduced by Hinselmann in 1927 which has never been very popular in this country.
2) The tincture of iodine and potassium iodide test of Schiller has little value other than suggesting promising points for biopsy in early stages of cancer with no gross lesion.
3) Still another recent advance and one to be discussed in more detail in this

*Read at meeting of the Orleans Parish Medical Society November 10, 1947.

paper is the test developed by Papanicolaou and Traut published in 1943. They established that cancer is an exfoliative lesion and it is possible to demonstrate it in a vaginal smear. This test cannot take the place of biopsy in decisive diagnosis of cancer, its chief function being a screening test in the search for cancer on a large scale in ostensibly normal women. It requires a trained cytologist.

4) Biopsy remains the one positive diagnostic procedure.

A lack of knowledge of these methods and their utilization by the medical profession is a contributing factor in the high mortality from cancer.

SMEAR TEST

The diagnostic value of the smear test as described by Papanicolaou and modified and improved by several authors since its original conception, is based on the constant exfoliation of malignant neoplasms which have a free surface, the cells becoming detached singly or in clusters. Small fragments of tissue in the form of cell cluster are found frequently in cancer smears and indicate exfoliation and they retain structural characteristic of the neoplasm.

The size and form of the nuclears are not significant. The cytoplasm of the undifferentiated cancer cells is usually basophilic but in some differentiated cells it is strongly acidophilic. The form of the cancer cell depends on the prevailing type of cancer. When cancer cells appear in clusters they offer additional proof of the diagnosis.

The advantages of the smear test are:

(1) Simplicity and inexpensiveness. (2) Reliability in hands of experienced men. (3) Permits early recognition of incipient cases in situ. (4) Can be carried out on a large scale. (5) It does not conflict with any established methods of pathologic diagnosis such as biopsy or curettage. (6) May reveal cancer where biopsy has failed and *vice versa*. (7) Used in follow up to determine progress of irradiation or other therapy.

The main disadvantages are (1) Criteria not yet clearly outlined. (2) Type and origin of malignant cells are not always clear. (3) Does not show grade of malignancy. (4) Does not give information as to mitotic activity. (5) Takes longer time for examination of smear.

The principle of the smear is that the vaginal secretion aspirated contains a mixture of normal cells, mucus, leucocytes and blood, and also specifically malignant cells exfoliated from any growth which may be present in the genital tract. Therefore, periodic vaginal smears can easily be suggested to women as a method of combatting cancer.

The cytology smear is really a "surface biopsy." The smears taken from the cervical os give a more rapid and more efficient identification of the malignant cells as 80 per cent of genital malignancies arise from the cervix or endometrium. In cervical malignancy the smears are taken directly from the surface of the growth, whereas in fundal carcinoma larger numbers of malignant cells will be found in the mucous at the cervical portal than would be disseminated over the more capacious vaginal floor. It is well worth the effort to insert a speculum and take the smear from the external os.

Cutting operations through a cancerous lesion carry the hazard of trauma, bleeding and lymphatic extension. It is better to confirm the malignancy preoperatively by a cytology smear, and after a positive diagnosis do a biopsy and give treatment accordingly. Sepsis presents a definite contraindication to a surgical biopsy.

In a patient with a positive Wasserman and a cervical lesion, clinically suspicious of malignancy, smears render helpful differentiation.

Technic of making smears: This technically simple method of making a presumptive diagnosis of uterine cancer in daily office practice makes the early discovery of female genital malignancy practical. The technic for taking vaginal smears is described by Papanicolaou. A slightly curved glass pipette, 8 inches in length, is attached to a 3 inch rubber suction bulb. The pipette must be absolutely dry and the patient must

not have douched the same day. Water destroys cellular details. Material is removed from os or fornix. The material is blown on a slide which is immediately dropped into a bottle of fixative ½ ether and ½ 95 per cent alcohol. Do not allow to dry on slide. Fix for five minutes. At this point the specimen may be sent to a cytology laboratory. The rest of the process of staining follows: Wash through 70 per cent —50 per cent alcohol to distilled water. They are then stained with Harris hematoxylin dipped four times in 5 per cent solution hydrochloric acid, washed in running tap water and placed in 5 per cent solution lithium carbonate for one minute. The slides are washed again in running tap water, rinsed in distilled water, and run up through the alcohols (50, 70, 80 to 95 per cent alcohol.) They are then stained for one minute in a 0.5 per cent solution of Orange G in 95 per cent alcohol. The smears are next washed in two changes of 95 per cent alcohol. They are stained in Ea 36 to 2 minutes, washed in three changes of 95 per cent alcohol, run through absolute alcohol to xylol, and mounted in Canada balsam.

In any clinically suspicious case one negative smear cannot be depended upon to exclude the presence of cancer.

Low power microscopic examination shows usually:

(1) Large number of leucocytes chiefly polymorphonuclear.
(2) Numerous bacteria.
(3) Red blood cells are usually found with loss of clear cut outlines appear crenated, degenerated or as shadow form.
(4) The degree of cornification is frequently higher.
(5) Histiocytes very common large foamy cells, multinucleated cells whose cytoplasm engulfs leucocytes, cellular debris and red blood cells.
(6) Bizarre cellular form cytoplasm is hyperchromatic, contains deeply stained granules. Vacules are frequently found with ingested cellular debris. Cells with arrested phases of mitosis.

The spatula technic as developed by Ayer can also be used, which is a means of collecting the cells before their exfoliation. This is done by utilizing a small spatula to scrape gently the surface of the tissue at the precise squamocolumnar junction. The cells and secretion are then transferred to a glass slide and the smear is prepared in the usual fashion. This method permits selectivity of cells collected so that a large concentration of squamous cells from the key point may be studied while still in an excellent state of preservation before they have shrunken or degenerated. A hook end spatula is used in a rotary movement, to obtain material after the mucus has been removed as in the Papanicolaou manner. This causes mild bleeding which is harmless and transient.

It must be emphasized that cytological practice requires highly specialized technic with care and precision in taking of test, skill in staining with excellent Papanicolaou stain, and experienced judgment on the part of the cytologist. Hunter and Ayre also developed centrifuge cytology technic, by gathering up the sediments from the bottom of the bottle. The specimen is centrifigued, then mounted in paraffin, sectioned and stained.

BIOPSY METHODS

Biopsy for obtaining material for study of carcinoma in office practice can be carried out in several ways. For study of intrauterine lesions all that is needed is to secure two or three small strips of endometrium which may be readily obtained with a long curet or a hollow suction curet such as that devised by Novak and by Randall. With patient in lithotomy position, a careful bimanual examination is made. The cervix is exposed with a speculum. An antiseptic is applied to the cervix, which is grasped with a single-toothed volsella. A uterine probe may be inserted to determine the length and direction of the uterine cavity, but this is not essential. Then the suction curet is gently introduced past the internal os up to the fundus of the uterus. The curet is gently but firmly pulled down along the anterior uterine wall until it reaches

the internal os. Then it is pushed back into the uterine cavity and turned to one side or the other and again withdrawn gently but firmly against the uterine wall and removed from the uterus. The cutting edge of the curet is then inserted in a small bottle of formalin or other fixing fluid and on blowing at the other end of the curet, two pieces of endometrium will be forced into the fixing fluid. The Novak and Randall curets are suction curets, but they may be used without suction, as just described. The pieces of endometrium removed must be stained and studied microscopically.

Tissue from the cervix can also be obtained in the office. There are special punch instruments devised for securing a good sized piece of tissue for diagnosis. To study the cervix, a tenaculum is applied to a healthy part of the cervix and not to the area under suspicion. With a sharp scalpel, a piece of tissue is excised which includes not only the entire area under suspicion but also at least 1/4 inch of healthy tissue all around it. The piece should be at least 1/8 inch deep if cut at right angles or at least 1/4 inch deep if cut wedge-shaped. The tissue should be placed in formalin or other fixing solution immediately. Bleeding may be checked by cauterization or by a small vaseline pack. Both of these methods may cause hemorrhage, infections or metastasis and are preferably done in a hospital.

SUMMARY

An attempt has been made to describe the technic that can be used in office practice in diagnosing carcinoma of the female genital tract by the general practitioner, and to give the principles involved, as well as the pathology. An evaluation of each method is given.

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THE USE OF BIOPSY IN UROLOGIC PRACTICE*

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Early and accurate diagnosis is of utmost importance in the treatment of urologic malignancies. The extent and nature of every tumor must be established to insure the most effective form of therapy. Although the location and extent of a tumor can usually be determined clinically, histologic study is the only way that the true pathologic characteristics of a tumor can be established. Accurate diagnosis is particularly important in the early stages of cancer since these are the only ones which are truly curable. The exact pathologic diagnosis of tumors is often extremely difficult even under the best circumstances. A gross description of the lesion, its extent and location and similar clinical data given to the pathologist will often be of great assistance in evaluating the microscopic picture. It is no longer feared that the incidental trauma associated with removal of material for biopsy tends to cause dissemination of a tumor. This has never been proved, but even if it is a possibility, it would not preclude the taking of a specimen for biopsy because at present this is the only means by which an accurate diagnosis can be made.

Tumors of the bladder are the commonest urinary tract malignancies. These lesions, which usually give rise to intermittent, painless gross hematuria, are discovered by cystoscopic examination and specimens for biopsy are taken from all suspicious areas. The specimen is taken with flexible forceps passed through the operating cystoscope, or else with the Stern-McCarthy resectoscope. The latter method is often preferable, for a larger and more representative sample of tissue may be obtained. All specimens are submitted for histologic study, with particular emphasis

*Read at the meeting of the Orleans Parish Medical Society, November 10, 1947.

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on grading. The grade of the tumor, its nature, its extent, and its location are the four most important points to consider in determining the type of therapy to be employed.

Carcinoma of the urethra is a more common condition than is generally supposed. This is especially true in women. The cardinal symptoms are frequency, burning, bleeding and pain, which occur early in the course of the disease. In the male, obstructive symptoms are produced by those lesions deep in the urethra, and the condition often is treated as a benign stricture until swelling of the penile shaft suggests a malignant growth. Biopsy and the operative removal of these lesions are relatively simple and the possibility of a clinical cure is often good.

Cancer of the penis is responsible for about 2 per cent of malignancies occurring in the male. It is limited almost exclusively to uncircumcised individuals. Prophylactic circumcision of all healthy male babies would greatly reduce the incidence of this form of cancer. The lesion usually begins in the coronal sulcus and is hidden by the prepuce. Phimosis and retention of smegma appear to be important causative factors. Specimen for biopsy is easily taken from the surface of these lesions, and biopsy should always be done to rule out malignancy in chronic, sloughing or proliferative penile sores.

Cancer of the testicle usually occurs in men under the age of forty. These tumors as a rule are highly malignant. Fortunately, they are not common, representing about 4 per cent of all tumors in the genitourinary system. Though many of these tumors are embryonic in nature and a positive Aschheim-Zondek reaction may be obtained, this test is not to be relied upon, chiefly because of the danger of false negatives. A highly malignant tumor may not give a positive reaction. A far better method of diagnosing these tumors is to expose the testicle surgically, obtain a biopsy specimen and submit this to frozen section; if the section is reported malignant, orchidectomy with high ligation of the cord can be immediately performed. An aspirating needle should never be employed to obtain a specimen for biopsy.

Carcinoma of the scrotum, once common among the chimney-sweeps of England, is now relatively rare. It seems prone to occur in paraffin, tar, and dye workers. The growth usually begins as a wart or ulcer and is similar to carcinoma of the skin occurring elsewhere. It grows slowly and metastasizes relatively late. Suspicious lesions here as elsewhere require biopsy.

Carcinoma of the prostate is usually so far advanced when discovered that a complete cure in a strict clinical sense is impossible. In these cases transurethral resection relieves the patient's urinary symptoms. Orchidectomy and endocrine therapy will in many cases prolong life and contribute greatly to the patient's comfort. All tissue removed in the course of resection for supposedly benign hypertrophy should be examined in an effort to detect any localized areas of malignancy which may have escaped clinical notice. In small early carcinomas of the prostate perineal prostatectomy offers the only chance for complete cure. Biopsy specimens of rectally palpable nodules on the periphery of the prostatic capsule should not be obtained by needle puncture as the chance of not obtaining a representative sample of malignant tissue is too great. A far better plan is to expose the gland perineally. A frozen section of the suspicious nodule is obtained and radical perineal prostatectomy is immediately done if a histologic diagnosis of malignancy is made.

Recently, Papanicolaou[1] has developed a method of detecting neoplasms of the urinary tract by a study of cells in the urinary sediment. The technic is much the same as that used in the study of vaginal smears for the detection of uterine carcinoma. A similar approach to prostatic cancer by studying prostatic secretions is being tried by Herbut and Lubin.[2] Neither of these methods is a substitute for biopsy and must only be considered as an adjunct to it. Both methods require special staining and as yet are in the experimental stage. However,

by virtue of their simplicity they may eventually be of great value in cancer detection clinics as screening methods for singling out early carcinoma of the urinary tract.

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BIOPSY (PROCTOLOGY)*

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Rich are the rewards of early diagnosis of cancer of the anus, rectum and sigmoid colon. Richer are the rewards of early diagnosis of precancerous lesions about these parts, because of the ease or facility with which so many of them can be removed in comparison to major type surgical procedures necessary for complete eradication or removal after they have undergone malignant changes. These latter operations are often mutilating in character and frequently are done to no avail as incomplete removal, or metastases, or both, preclude a favorable outcome. To put it differently, early operations on precancerous lesions are usually simpler, safer, easier on the patient and prevent the later necessity for major surgery.

These points cannot be over emphasized because so many patients have a tendency to procrastinate if told their lesion or trouble is not cancer but is a precancerous one. Many, if told it is not yet a cancer are willing to postpone the surgery required.

In proctology, as much as in any other field, biopsy is an important adjunct in the diagnosis, or ruling out of malignancy, of all doubtful lesions in and about the anus and rectum. In some, biopsy is the *sine que non*. Biopsies in proctology have immense value in differential diagnosis. Too often there is the feeling or attitude toward biopsy that its usefulness is limited to a green light or go-ahead signal for surgery. Not enough emphasis is placed on its usefulness at times in changing a diagnosis whereby lesions (amebomas, etc.) which are amenable to medical or non-operative measures are not subjected to major surgical procedures. Some conditions that are at times mistaken for malignant ones include lymphopathia venereum, tuberculosis ulcerations and proliferations, perianal chancres, anal fissures, polyps, enlarged anal papillae, fistulae, and hemorrhoids,—thrombosed, eroded or ulcerated. These are diagnosable by their clinical appearance and a biopsy is not often required. But if doubt exists after thorough examination, always biopsy them.

The collection of specimens for biopsy in the field of proctology follows the usual practices for the collection of good biopsy specimens generally, with modifications necessitated by the differences in the anatomy of the region and the problems of endoscopic manipulation of the biopsy forceps or collecting instruments. At least two specimens should be obtained, one from the center of the mass or ulcer, and one from the edge, which means a section extending from the pathological into normal tissue, in other words, from the transitional zone. The section may be a thin one but should be relatively deep to reveal the subsurface changes that are often of diagnostic import. If the lesion is large, sections from several areas should be obtained. Hemostasis should be thorough before the patient is allowed off the table. Most bleeding will check spontaneously but it is unsafe to place complete reliance on this. At times troublesome bleeding continues and requires more active measures for its control, such as pressure with cotton (plain or soaked in astringent solution) or electrodessication. The newer hemostatics such as Gel-foam and Oxycel may be used. Some say that bleeding is never troublesome following biopsy, but this is an over-statement as at times bleeding is sufficient in quantity to alarm the patient and to tax the ability of the surgeon to control it, especially in high-lying lesions where the blood and clots obstruct the view of the bleeding point or points and movable lesions such as pedun-

*Read at meeting of the Orleans Parish Medical Society, November 10, 1947.

culated polyps recede and rotate, thus changing the presenting surface.

Reference has been made to endoscopic specimens. This naturally entails the use of the procto-sigmoidoscope. Details of the use and manner of passage of these instruments are beyond the scope of this discussion, but one point should be mentioned here relative to the type of procto-sigmoidscope used. Instruments with the illumination or electric bulb at the distal end have less shadows than those with proximal-end illumination which allows the biopsy forceps to be interposed between the source of light and the lesion.

There are many lesions which are easily accessible and about the nature of which we are relatively certain from the clinical picture they present. This group includes non-malignant entities such as hemorrhoids, enlarged papillae, fissures, fistulas, fibrous polyps; and another group such as epitheliomas of the malignancy, of which there is little or no doubt. Instead of obtaining a biopsy specimen and then operating, one procedure should be employed and that one should be complete surgical eradication of the lesion or lesions and all tissue should be sent to the pathologist for complete study. This often saves the patient an extra operation and has great value in affording the pathologist larger and better specimens with which to work. All tissue removed at operation even when not considered malignant clinically should be sent to the pathologist routinely because reports of unsuspected malignancy have often been returned on what had appeared to be non-malignant tissue.

Whenever there is any doubt concerning the true nature of an anal or rectal lesion, a biopsy specimen should be taken for examination. Where clinical diagnosis of carcinoma has already been made, biopsy should be used for confirmatory proof, and to classify or grade the malignancy of the tumor for prognosticating the end-results and to assist in making a decision as to methods of treatment,—surgery or radium,—because low grades of malignancy by Broder's classification are better handled by surgery and the higher grades by radium. However complete reliance cannot always be placed on biopsy classification of grades of malignancy. This is as true in proctologic specimens as in those from other regions.

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A NEW RETRACTOR FOR USE IN THYROIDECTOMY

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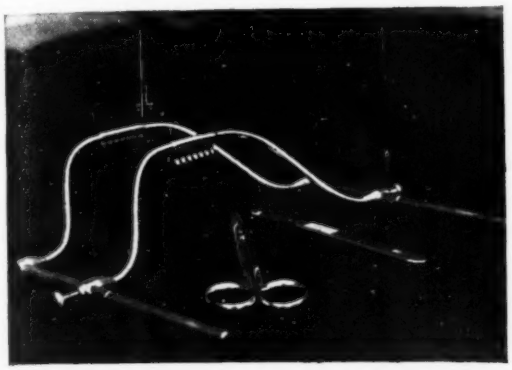
One of the most widely employed instruments for retaining the skin flaps open during thyroidectomy is the Beckman retractor. I have used it for years but it has repeatedly manifested a number of defects. Two of the most obvious are that it frequently slips out of position and its extended handles get in the way of the assistant.

The instrument herein presented is intended to overcome these faults. I devised it with the idea of having something recessed and unobtrusive to securely hold open the skin and subcutaneous tissue.

It consists of two 1/4 inch round rod tracks on to which is firmly affixed a curved sustaining rod coming off the ends at an angle of 44°. This sustaining rod, made of 3/16 inch steel is so curved as to conform to the base of the neck and chest. In the center of this rod are affixed claws for retracting the skin. Another curved sustaining rod is movable on the tracks being affixed to sliding cylinders. This rod likewise has claw retractors in its center. The curves of the sustaining rods permit a minimum of the instrument to be present in the field of operation and the design is such that the main portion of the instrument is recessed into the lateral spaces around the neck. After the wound is opened the retractor claws are placed under the skin flaps and the retractor is separated. The desired width of the opening is held secure by thread screws.

The use of this instrument in a number

of cases has proved it to be most effective and very secure.*



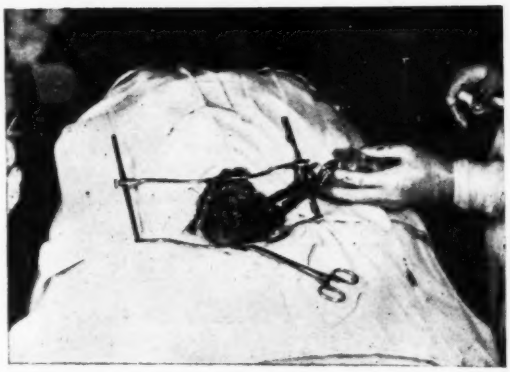


Fig. 1. a.) Self-sustaining retractor for skin flaps in thyroidectomy.

b.) The retractor in use as seen from above.

c.) The retractor in position, shown from a side view.

*The retractor will be produced by A. S. Aloe Co., St. Louis, Mo.

SALMONELLA BLEGDAM INFECTION A REVIEW OF LITERATURE AND REPORT OF A CASE

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The first case of Salmonella blegdam was reported in 1935 from Blegdam hospital, Copenhagen. A second case was reported from Shanghai about one year later. In December, 1944, fifty cases of proven Salmonella blegdam infection were reported from New Guinea, Buna, and Bougainville by medical officers of the Australian army located in that area. Another series of fifteen cases was reported in the Australian forces in New Guinea and Buna subsequent to the above date. About the same time, five cases of natives of the island were found, manifested by enteric like fever. In the same group, one fatal case was reported in a Japanese prisoner of war. The case which follows is the first from which the organism has been cultured in the United States.

Symptomatology of the enteric fever was divided into three categories:

1) Simple diarrhea with stools containing mucus, with nausea, vomiting and abdominal pain.

2) Salmonella fever resembling typhoid fever, showing hyperpyrexia, malaise, leukopenia and a slow pulse rate. Forty-five per cent of the cases reported exhibited this syndrome.

3) Salmonella fever with septic complications, the organism spreading through the blood stream and localizing in various parts of the body.

During the first two weeks, the course resembled Salmonella fever. From there on various manifestations occurred including cystitis, peritonitis, perichondritis, epididymo-orchitis, abscess of the buttocks, cholecystitis, pericarditis, ureteritis, empyema, and bronchopneumonia. The salient features are an incubation period of approximately two weeks' duration, fever, toxemia in all cases plus a slow pulse rate; in 12 per cent a skin rash consisting of rose spots or macules on the abdomen, arms and legs. Abdominal distention, doughy abdomen, abdominal tenderness, and diarrhea were usually present.

REPORT OF CASE

A 25 year old white female was first seen by Dr. Henington on November 11, 1947. At this time, the patient had a weeping erythematous dermatitis in both popliteal fossae and on the anterior and posterior surfaces of each thigh. This had been present for two weeks; the temperature was normal; there was no adenopathy; and the throat was clear. A tentative diagnosis of dermatitis venenata was made. The patient was given a soothing compress of 4 per cent boric acid followed by a shake lotion. During the period of two weeks, eruption became worse and spread to other parts of the body. The weeping had stopped, and the eruption was simply an erythema and scaliness not unlike the rash seen in scarlet fever. There were no petechiae and no vesicles.

The patient was admitted to the dermatology service because of the severe skin lesions. The family, medical and surgical histories were negative. General physical examination was negative, except for bilateral palpable inguinal nodes and skin lesions as described above. A tentative diagnosis of severe, allergic, pruritic dermatitis was made.

Course in Hospital: The patient's temperature was 100.2. There were three bouts of fever; the first of which reached 104.4° F, the second, twenty-four hours later reached a peak of 103.4° F, and the third lasted for three days reaching peaks of 104.8, 105.2, and 105.4° F, on successive days. The first and second febrile reactions occurred on the third and fifth hospital days, and the third occurred on the tenth hospital day. Temperature fell by lysis after the second and third bouts of fever.

Blood cultures were taken at the height of the fever and were overgrown by contaminants. Agglutinations were negative, and all other laboratory work including urinalysis and stool examinations were within normal limits. The total white count reached 11,000, and the patient developed a rather severe anemia following the third febrile reaction. A stool culture taken at the height of the fever revealed Salmonella blegdam.

The hyperpyrexia was controlled with alcohol sponges, cold enemas and cool wet sheets. On the fourteenth hospital day, the characteristics of the rash changed somewhat and resembled that of scarlet fever.

Treatment included penicillin 50,000 units q.3.h. for nine days after admission with no apparent improvement. Pyribenzamine, 100 mg. was given q.4.h. until the eleventh hospital day. Streptomycin 5 Gm., q.4.h., was begun on the eleventh hospital day, decreased to 2 Gm., q.3.h., next day, and was discontinued several days later. Para amino benzoic acid, 2 Gm., q.4.h., was begun twenty-four hours after streptomycin was increased 2 Gm., q.2.h. the following day and was discontinued five days later. Twenty-four hours after para amino benzoic acid was begun the temperature became normal and remained so.

The patient was discharged on the twenty-second hospital day.

An attempt was made to determine the origin of the patient's infection. Her husband was stationed in the Southwest Pacific and Japan during the war. Several stool cultures run on him were reported negative for Salmonella blegdam.

Attempts to agglutinate the original culture of Salmonella blegdam with the patient's serum were unsuccessful six weeks after discharge. Failure to agglutinate the organism might be explained by the length of time which had elapsed before test was attempted.

Since the organism was isolated by the pathology department at Southern Baptist hospital, the same organism has been isolated by the pathology department of Touro Infirmary from a blood culture of a patient of Dr. M. Loeber and Dr. J. L. Dyer. The serum of this patient showed a significant agglutination for Salmonella blegdam when it was checked several weeks later.

Note: The author wishes to express his appreciation to Dr. V. M. Henington and Dr. W. H. Gillentine for their assistance and permission to report the case, and to Dr. M. Loeber and Dr. J. L. Dyer for permission to mention a similar case which was treated by them.

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BILATERAL BRODIE'S ABSCESS REPORT OF A CASE

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A review of the literature for the last five years failed to reveal any reported cases of bilateral Brodie's abscess, and the following case is considered, therefore, of sufficient rarity to warrant reporting.

CASE REPORT

A 19 year old boy entered the hospital because of recurrent pain in the right ankle of over four months' duration. The pain, deep, and of a boring quality, was made worse by weight-bearing, and he had worn crutches for the previous three months. Three weeks before admission the ankle had become swollen and was lanced by a local

physician. The wound was made on the lateral aspect and yielded sanguine-purulent material. The drainage continued until admission. One week previous to admission the medial aspect of the ankle became similarly swollen and painful, but to a lesser degree than the lateral side. The patient further stated that when the ankle was causing the most pain, he could palpate "kernels" in the right groin and behind the right knee.

A review of the past history elicited an episode similar to this eight years previously. The disorder subsided spontaneously at that time and gave no further trouble until the onset of the present illness. There was no obtainable history indicative of acute osteomyelitis at any time.

Physical examination was negative except for the right ankle. This was swollen and dusky in its entirety, but most markedly on the lateral surface. Here over the malleolus there was a draining sinus emitting grumous discharge freely. Pain and tenderness were noted, and it was observed that the patient was completely disabled.

X-rays showed a cavity in the centre of the tibial shaft at its lower extremity with an area of destruction extending to the lateral cortex.

The patient received penicillin 15,000 units every four hours for ten days (900,000 units) and was then deemed ready for surgery. Under general anesthesia (ether, open) the lower end of the tibia was approached through a three inch incision in the medial side of the ankle passing anteriorly above and below the internal malleolus. The periosteum was found to be greatly thickened, and the bone was honeycombed from a point just above the internal malleolus upwards for a distance of one and one-half inches with extreme roughening of the cortex. The bone cortex covering the Brodie's abscess was chiseled away and considerable granulation tissue, grayish in colour, jelly-like in consistency, curetted. A diverticulum which admitted the fingertip led away distally and medially from the main abscess cavity to open into the soft tissues behind the malleolus. Curetting here also yielded granulation tissue, and a hemostat was pushed through from the abscess cavity to the surface, cut down upon, and a rubber drain brought through. The cavity itself was dusted with sulfathiazole crystals (about 3 grams) and packed open with vaseline gauze. Convalescence was uneventful.

Dr. A. J. Flack, Director, Institute of Public Health, Faculty of Public Health of the University of Western Ontario, reported on the specimen as follows: "The specimen consists of a number of grayish red pieces of soft tissue with some irregular bony fragments. The pathologic condition is Brodie's abscess. Sections show the abscess cavity to be partially lined by granulation tissue and in the wall there is a proliferation of connective tissue which shows a moderately dense infiltration of plasma cells, lymphocytes and polymorphonuclears. The microscopic picture is that of a chronic abscess and is compatible with that of Brodie's abscess. There is no evidence of malignancy."

On second admission six months later the patient complained that he had sprained his left ankle twice in rapid succession about one month before admission. Since that time he had experienced some pain and disability with slight swelling of the joint. He was afebrile.

Roentgenograms of the extremity revealed a

Fig. 1—X-ray made on first admission showing bilateral lesions.

Brodie's abscess in the left lower tibia with slight elevation of the medial periosteum. The original plates were then consulted, and a previously missed area of rarefaction surrounded by eburnation was demonstrated in the same position as that occupied by the lesion noted on the new plates.

Therapeutic management was similar to that noted above and the postoperative condition was excellent with the patient being discharged on the sixteenth postoperative day. The report of the pathologist again confirmed the clinical diagnosis.

The patient continues symptom-free three years postoperatively.

The therapy of these cases has been re-

cently reviewed by Buchanan and Blaire. In their series of cases, the best results follow pre- and postoperative penicillin administration. The operative measures are saucerization of the focus with primary closure of the operative site. This is in agreement with the therapy preferred by the English authors (Illingworth, et al; Bailey and Love).

In the *Medico-Chirurgical Transactions* of 1832, Mr. (later Sir) Benjamin Brodie, Surgeon, St. George's Hospital, London, first described a "circumscribed abscess lined with a granular membrane surrounded by sclerotic bone". He pointed out at the time that an abscess may occur in the interior of any bone, but according to his experience it is more common in the tibia than in any other bone. He gave a brief account of eight cases.

Chronic foci remaining after an episode of acute osteomyelitis have been reported as Brodie's abscess, but the abscess as originally described begins as a chronic process. It is true that it may show its relation to the usual forms of bone infection by occasionally developing a more acute course than previously. It is for these reasons that Hertzler advises that the term "false Brodie's abscess" be applied to those following acute infections. Henderson and Simon found that of 145 cases of bone abscess, only 23 were true Brodie's abscesses. We may presume the lesion to be an unusual, if not rare, one.

There is yet a third contender for the title of Brodie's abscess. Phemister has described localized areas of fibrous or granulation tissue which he chooses to call "chronic fibrous osteomyelitis". The failure to cultivate bacteria from such areas does not rule out their probable infectious basis, and these areas deserve, probably more than those abscesses following acute osteomyelitis, to be called Brodie's abscesses.

The discoverable pathology is that of an attenuated infection with a mild reactive process, granulation tissue formation, and the deposition of new bone. The latter finds expression more by a sclerosis than by an increase in volume, although the bone often may be thickened about the site of disease. At operation, the increased resistance offered the chisel confirms the diagnosis before the abscess is reached. The abscess itself is usually small, varying from 0.25 cm. to 2.5 cm. in diameter. The cavity is filled with a granular material containing small particles of bone, but seldom true bone spicules. In older abscesses the center of the lesion may be clear and the walls lined with a membrane suggesting a bone cyst. However, abscesses are always unilocular and surrounded by sclerotic bone; cysts, on the other hand, are multilocular and usually surrounded by rarified bone.

Histologically the early cases are characterized by the presence of granulation tissue comprised largely of plasma cells, but leukocytes are abundant. In cases of longer duration there is a definite pyogenic membrane with the typical fibrous tissue wall and granulation tissue lining. The bacteria found have been most commonly staphylococci, less often streptococci, and in rare instances, hemolytic streptococci (Wilensky). In the case of Phemister's "chronic fibrous osteomyelitis" leukocytes and lymphocytes may be absent and the tissue resembles the lining of bone cysts. In some cases giant cells may be found. It is upon the latter finding that Barrie bases his contention that giant cell tumors are primarily inflammatory in nature.

Ogilvie suggests that the primary lesion is a strain of the extremely vascular juxtaepiphyseal region coupled with a general lowered resistance in the presence of foci of infection elsewhere.

Similar to acute osteomyelitis, the disease is one of adolescence, but owing to its chronic, non-debilitating nature, it may not be discovered until adult life.

The onset is usually slow in character and the most common symptom that of deep, boring pain, often, as is characteristic of bone pain, worse at night. As the focus is frequently near the epiphyseal line, joint pain is simulated frequently. Tapping over the site of disease is painful, but periostitis is rare. In some cases ex-

udation into the joint and swelling of the soft parts may be seen. In most cases a swelling of the bone (which can often be ascertained by simple palpation) and eburnation of the bone about the abscess occur. The latter may achieve such density that the underlying cavity fails to visualize on the roentgenogram.

The course of the disease is characterized by intermittent bouts of pain—increasing in severity and usually near the end of a long bone—which is usually insufficient to disable the patient. Fever is seldom present. After a free interval (sometimes months in duration) the pain returns for a few days or weeks. The condition is often considered to be rheumatic, and the course may continue, as in one case reported, for more than fifty years. In the most acute cases, the patient may show a hot, red, tense, fluctuant swelling, with some edema of the affected limb.

The location and size of the abscess can usually be made out on the x-ray plate, but in some instances it is too small and it may be overlooked, especially if the plate is developed too darkly. Rigler describes the roentgenologic appearance as being a "localized defect near the end of a long bone surrounded by a zone of sclerosis or increased density". He further states that the differentiation from tuberculosis may be difficult.

Statistically, the tibia seems to be the most frequently involved site. This confirms Brodie's original observation. Hertzler cites Koenig (Lehrbuch d. spec. Chir., 1865, Bd. 3, s. 540) as his source for the statement that 75 per cent of the abscesses occur in this bone. The proximal end is most frequently, and the diaphysis only occasionally diseased. Brailsford reports 40 cases of tibial involvement and 22 in other areas. The majority of cases occur between 11 and 30 years of age, and the male-female ratio is 2:1.

The differential diagnosis of Brodie's abscess includes bone cysts, chronic sclerosing osteitis, sarcoma, gumma, endothelial myeloma, and tuberculosis.

The bone cyst usually presents no symptoms of pain, a spontaneous fracture being frequently the first sign of this disease. In addition, roentgenology reveals no surrounding osteosclerosis.

Chronic sclerosing osteitis involves the medulla principally, giving rise to a spindle-shaped bone with a thickened cortex, narrowed medullary cavity, and no typical area of rarefaction.

The usually abrupt onset of sarcoma with its typical roentgenographic appearance of an extensive and destructive process without regularity of outline differentiates this condition with ease.

The massive reaction of adjacent bone characteristic of gummatous degeneration of bone, the persistent and intolerable night pains, and the positive serology make this diagnosis by no means difficult.

Tuberculosis of the bone is destructive and leads to the early formation of sinuses and sequestra and there is no eburnation of the surrounding bone.

A careful history, physical examination and roentgenologic study will rule out the arthritic conditions.

The discovery of an osteoclastoma at this stage would be purely accidental, for the signs and symptoms are negligible. The radiographic appearances are quite similar, and therefore, the clinical history would be necessary for differentiation.

The course of the myeloma is far more rapid than that expected of a Brodie's abscess as is revealed by the history, and serial radiographic study or biopsy will provide the diagnosis.

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INTRATRACHEAL ANESTHESIA—ITS USES AND ABUSES*

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It is not difficult for even an anesthesiologist to understand why there might be an aversion to intratracheal anesthesia in some medical circles. This is largely because some of us have at one time or another witnessed an attempted intubation which would make Custer's last stand seem like an anemic affair by comparison. Moss[1] has stated, "ploughing up the pharynx with a laryngoscope in an attempt to dig out an epiglottis from a pool of bloody mucous is one of the least inspiring sights of modern anesthesiology". We certainly agree with Moss. Memories of the occasional difficulties linger on; the times it has been employed uneventfully are forgotten and often never appreciated. Irrespective of the impressions one gains by casual observation it cannot be denied the technic is indispensable in certain surgical procedures which are attempted. The advantages of intratracheal anesthesia outweigh the disadvantages by far.

The chief reason for introducing an intratracheal catheter is to assure an unimpeded airway, or stated more simply, its primary purpose is to prevent the patient from choking to death either suddenly or slowly.[2] Mechanical obstruction, either existent or anticipated, is averted or controlled. Respiratory movement in awkward positions such as the prone or lateral are aided.

In addition, the intratracheal technic allows the anesthetist to withdraw from the operating field when he must struggle with the surgeon for it. Thus, not only is the surgeon assured of asepsis, but he also has non-interference with his work without jeopardy to the patient. Then also, the intratracheal catheter may be so arranged that a tight seal results between it and the tracheal wall. The patient is thus protected against entry of foreign matter such as vomitus, pus, blood, or mucus, into the trachea. Likewise, suction is available directly for the respiratory tree. This is indispensable when purulent secretions are present. Furthermore, the intratracheal catheter prevents annoying reflex laryngospasm seen most frequently in upper abdominal and intra-thoracic surgery. The advantage of control of pulmonary ventilation in thoracic surgery and the availability of positive pressure are further desirable features obtained.

The disadvantages of intratracheal anesthesia are twofold: the process of intubation may be time consuming and the procedure may be traumatic. Intubation involves in many instances a longer induction period as deeper anesthesia is usually necessary for relaxation and obtundation of pharyngeal and laryngeal reflexes. This disadvantage, probably one of the most annoying to impatient operators, is more than offset by the safety the free airway affords. An experienced anesthetist can intubate in the time required by a neophyte to produce the necessary induction. Gillespie[3] has stated "it is wise to regard intubation in the light of prophylaxis rather than treatment—intubation during anesthesia is tantamount to confession of faulty judgment of that case."

The degree of trauma inflicted varies directly with the experience of the anesthetist. On this experience depends the incidence of minor respiratory complications. Mature medical judgment is necessary for an anesthetist to decide whether the advantage of endotracheal anesthesia will outweigh any possible disadvantage in his own hands.

The uses of intratracheal anesthsia parallel its advantages, and are peculiar to operations on various portions of the body.

HEAD and NECK: Intratracheal anesthesia is particularly desirable in opera-

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*Read at meeting of the Orleans Parish Medical Society, November 10, 1947.

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tions about the head and neck. In certain instances, particularly in procedures of short duration, intubation may not be necessary and justified. However, since one cannot predict when obstruction may occur, one is justified in intubation of all such cases. In otolaryngological, oral, and neck operations, the anesthetist is able to withdraw from the operative field and still have full control of the patient. In intracranial surgery, one is at ease when an intratracheal airway is in place. Central vomiting and respiratory failure peculiar to operations of this type are more easily managed. Some difference of opinion exists regarding surgery of the thyroid gland. Thyroid surgery usually falls into three classes in respect to the type of anesthesia employed. Certain operations on the gland are done primarily for relief of obstruction due to pressure of the gland on the trachea. All patients undergoing surgery for this cause should be intubated. Patients with goiter who do not have symptoms of obstruction or toxicity may not necessarily require intubation. The decision to intubate or not to intubate depends upon the difficulties arising during induction and the ease with which the airway is maintained without obstruction. However, since one cannot anticipate obstruction, the more conservative stand is to intubate. The good anesthetist is not the one who knows how to get out of trouble, but the one who knows how to avoid it. Thyrotoxicosis always presents a difficult anesthetic problem. The patient is usually a poor anesthetic risk who should not be subjected to deep anesthesia or trauma. However, without intubation laryngeal spasm from manipulation of the gland and trachea during light anesthesia may cause anoxia and carbon dioxide retention which are undesirable in the face of the increased metabolic rate and cardiovascular instability characteristic of these patients. Tracheitis from pressure of the gland may exist preoperatively. The presence of the catheter during the operation may aggravate the condition, particularly if there is excessive manipulation and motion of the trachea. Certain operators still adhere to the unreliable custom of attempting to avoid damage to the laryngeal nerve by listening for the phonation caused by touching it. Isolation of the nerve is preferred for absolute safety to avert this complication. Lahey is most conservative and prefers intubation for all neck surgery.[4] He advocates exposure of the nerve.

THORAX: Intratracheal anesthesia is indispensable for intrathoracic operations. Prior to the introduction of this type of anesthesia it was almost impossible to perform intrathoracic operations with satisfactory post-operative results. Not only are these operations difficult because the preexistent pathological processes interfere with proper pulmonary ventilation, but also positioning on the operating table interferes with adequate respiratory movements. In addition, mucus, pus, blood, and other secretions are usually present in the air passages and further interfere with adequate ventilation. The pneumothorax, although on one side, and the troublesome mediastinal shift cause further difficulties. Intratracheal anesthesia alleviates this by allowing the use of positive pressure, controlled or assisted respiration, and continuous suction. A further modification of the endotracheal technic seals off the bronchus of a diseased lung when copious purulent discharge is present and allows a relative degree freedom of contamination of the healthly lung.

ABDOMEN: Most abdominal procedures are easily performed without intubation. The experienced anesthetist is able to judge by preanesthetic examination or from the patient's reactions during induction whether or not intubation is necessary. Laryngeal spasm during upper abdominal surgery may interfere with adequate ventilation. Straining occurs during such spasm and may present technical difficulties for the surgeon. Likewise, relaxation is difficult to attain because the inadequate ventilation does not allow the requisite amount of drug to pass into the lung. Intubation absolves this difficulty. The routine use of intratracheal anesthesia by the "lazy" anesthetist because it requires less effort

and less attention to the patient than would be required by the ordinary technic is obviously an abuse of the method.

AWKWARD POSITIONS: When awkward positions are necessary for surgery, mechanical hindrance to the airway and poor approximation of the mask are frequent technical problems which make proper administration of anesthesia difficult. The skilled anesthesiologist is more able to control the patient without a catheter in place than the novice. However, he always resorts to its use in the prone position since this is the most difficult of all from the standpoint of anesthesia. Certainly the patient is entitled to the safety the intratracheal tube affords under these circumstances.

Other uses of intratracheal intubation, just to be mentioned, are in irremediable upper respiratory obstruction, for resuscitation, and tracheo-bronchial aspiration when atelectasis, pulmonary edema, and other similar clinical conditions arise. Its use in institutions where non-medical personnel administer anesthetics and the supervisor cannot possibly oversee each anesthetist is mandatory. One of the most difficult tasks that confronts the anesthetist is maintenance of a proper airway. Technician anesthetists do not always recognize obstruction to the airway. An intratracheal tube assures it and guarantees the safety of the patient.

Operations on infants are best done without intubation because of the softness and small size of the involved structures. The cross section of the trachea in infants is reduced in greater proportion by the cross sectional area of the wall of the catheter, regardless of its thinness. Secretions more copious in these subjects are removed with greater difficulty. Obstruction due to edema postoperatively may occur if any degree of trauma is inflicted.

It should be needless to say that intubation is a procedure to be attempted only by individuals who have been instructed in laryngoscopy. This is not always the case, however. In many localities not only are intubations attempted by individuals who know little more than the rudiments of anesthesiology but also by individuals who are not practitioners of medicine. We would be horrified at the thought of allowing a non-medical person attempt a bronchoscopy. Still, many of us have glibly allowed non-medical personnel to attempt intratracheal anesthesia. There is little difference between the introduction of a bronchoscope and the introduction of an intratracheal catheter except that in the case of the latter the patient is under anesthesia and is utterly defenseless to protest against the trauma inflicted as he would under local anesthesia during a bronchoscopy.

Most of the abuses of intratracheal anesthesia arise from lack of skill or from the exercise of poor judgment. Gentleness and proper relaxation are absolute necessities for intubation. The ability to decide when to go on, when the intubation is difficult, and when to stop are likewise esssential prerequisites. Here again mature medical judgment is necessary. When the nasal method is selected, the operator must consider the presence of infection, nasal spurs, and hyperplastic lymphoid tissue in the upper air passages. The presence of these may lead to lower respiratory infection, epistaxis, and adenoidectomy respectively. When the oral route is employed, the laryngoscope must not be pressed against the teeth to pry the jaws apart. A bite block should be inserted before the patient can bite the catheter or injure his own teeth. Most of these are technical details which are easily cared for by most anesthetists.

Extubation is equally as important as intubation, particularly when one considers that 50 per cent of all anesthetic accidents occur after the operation has been completed. Respiratory obstruction and aspiration of foreign substances at the time of tube removal are responsible for a great proportion of difficulties.

Objection has been raised to intratracheal anesthesia by individuals who are not anesthetists and who have had little or no experience with it on the

grounds that the presence of the tube in the trachea is "irritating". It is difficult to conceive how a soft rubber catheter introduced for several hours into the trachea can produce such an effect when a metal tube inserted in a tracheotomy remains for days without any apparent harm. It must be emphasized that the majority of deleterious effects which arise are from trauma due to "bungling" at the time of insertion of the catheter. The well-trained, skilled anesthesiologist is qualified to reduce these difficulties to a minimum.

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SPINAL ANESTHESIA FOR CESAREAN SECTION*

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Spinal anesthesia is gradually assuming its rightful place in surgery. Its limitations, dangers, as well as its advantages and indications are on the whole well recognized. Its use in obstetrics, however, is still a matter of considerable controversy. Numerous writers have called attention to the fact that its use is hazardous in operative obstetrics. Recently Greenhill[1] stated that of all anesthetics used for obstetrics it is the most dangerous. From collected statistics he has reported a maternal mortality rate of 1:456 attributable to the anesthetic. On the other hand, other authors have hailed it as the most suitable. Freiheit and Magnano[2] feel it to be the ideal anesthetic for Cesarean section. Arnell, in 1945, discussing a paper by Habeeb,[3] reported a maternal mortality of 20.8 per cent from spinal anesthesia for Cesarean section at the New Orleans Charity Hospital. Arnell's figure was computed from a series of 24 sections performed under spinal anesthesia during an eight year period. This is not a fair evaluation of spinal anesthesia for Cesarean section because the series is too small. His purpose, however, was to call attention to the hazardous nature of this kind of anesthesia. Those opposed to its use have gained their impression from one or two unhappy experiences. Exactly why it is hazardous, has never been well defined. Is spinal anesthesia more hazardous to the obstetrical than to the surgical patient? If it is, why is it? Can it be made safer? These questions coupled with the paucity of data on spinal anesthesia in obstetrics at the Charity Hospital, have stimulated our interest in studying the problem in more detail and elucidating its hazardous features, if any.

METHOD OF STUDY

Two hundred and eight Cesarean sections were performed under spinal anesthesia from January 1945 to September 1947. All the anesthetics were administered and supervised by the Residents in Anesthesiology at Charity Hospital. In deciding whether or not spinal anesthesia was suitable, the indications and contraindications followed in general surgery were applied to these patients. Those with cardiovascular disease, hypotension, anemia and other complications were excluded. The ages of the patients varied from 16 to 46. The majority were in their twenties and early thirties. Physical and laboratory findings were negative in 89 per cent of the cases. Seven per cent presented specific contraindications to spinal anesthesia. These were abnormalities in blood pressure, chiefly hypertension. The remainder presented complications which do not contraindicate spinal anesthesia, notably diabetes, pyelonephritis, hydronephrosis, early toxemia, and upper respiratory infection.

No premedication was given in 25 per

*Read at meeting of the Orleans Parish Medical Society, November 10, 1947.

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cent of the cases. The remainder received atropine or scopolamine in combination with a short-acting barbiturate or dilaudid, within the hour previous to induction of anesthesia. In 101 cases atropine or scopolamine alone was used.

The lumbar puncture was performed with the patient in the upright sitting or the lateral prone position, whichever was more convenient. The site of puncture was at the third or fourth lumbar interspace, whichever was more accessible. Immediately after injection of the drug, the patient was placed in the supine position with the head sharply flexed on a pillow. Ordinarily in general surgery, the patient must be placed in the dependant position to obtain the extent of anesthesia necessary for abdominal surgery. In obstetrics, if this is done, anesthesia extends to the upper spinal segments. Only in five instances was the Trendelenburg position necessary because the anesthesia was not high enough. In three cases in which the level of anesthesia extended beyond the 7th thoracic segment, the reverse Trendelenburg was necessary to prevent further cephalad migration of the drug. In all cases the anesthetic drug was given as a hyperbaric solution, made so by weighting it down with 10 per cent glucose. Pontocaine was used in 54 per cent of the cases, Nupercaine in 37, PT-19* in 5 and Novocaine in 4 per cent. Satisfactory anesthesia was obtained with much smaller doses than ordinarily employed in abdominal surgery. Doses comparable to those used in general surgery caused a "greater spread" and analgesia extended to undesirable heights. Untoward reactions appear to be more frequent when the dosage is excessive. Nupercaine was used in amounts varying from 5-7.5 mgm., Pontocaine 7.5-10 mgm., Novocaine 70-100 mgm. and PT-19 8-10 mgm. Immediately after induction of anesthesia, an infusion was started, primarily to assure having a vein available for the administration of vasopressor drugs, stimulants, or blood. Sixty eight per cent of the cases received 500 c.c. of blood in conjunction with an infusion of glucose while on the operating table.

The extent of sensory anesthesia ranged between the 10th and 7th thoracic segments in 94 per cent of the cases. In 3 per cent the analgesia was confined below the 10th thoracic segment. This level was not adequate for surgery. In 3 per cent of the cases analgesia extended above the 7th thoracic segment.

RESULTS

From the standpoint of surgery, the results were very gratifying. In many instances, however, there were tense moments for the anesthetist. Hypotension was a most constant and distressing complication. The blood pressure fell in every single case. In 31 per cent of the cases, however, the reduction in pressure was not severe and remained above 100 mm. Hg. systolic. In 69 per cent of the cases, the systolic pressure dropped below 100 mm. Hg. In approximately one third of these it fell to 60 mm. Hg. This fall occurred on an average of five minutes after establishment of anesthesia. It was precipitous, dropping abruptly, once it began to fall.

The hypotension was combatted by the use of ephedrine intravenously. In 14 cases a second dose was necessary because the pressure remained elevated only a few minutes and began to fall again. In four cases a third dose was administered because the pressure dropped again after the second dose. A combination of intravenous and intramuscular injection was used in 45 cases. As a rule, this is a very effective technic to employ. In 9 per cent of the cases ephedrine was administered five to ten minutes before anesthesia was induced. A blood pressure drop occurred in one patient in this group and intravenous ephedrine was necessary to restore the blood pressure to normal limits. In 13 per cent of the cases a hypotension appeared after anesthesia was established and the operation had been under way for some time. Clinical experience has taught us that this fall is due to fluid loss, trauma, or other

*B-(2-piperidyl)-ethyl o-aminobenzoate hydrochloride. Known under trade name of Lucaine.

factors. Vasopressor drugs are not effective at this time and may even be harmful. Blood and fluids were effective in overcoming this complication.

Immediately after delivery of the infant, the blood pressure rose, somewhat abruptly, to above pre-anesthetic levels in 78 per cent of the cases. The elevation averaged 10-30 mm. Hg. systolic. There was likewise a proportional rise in diastolic pressure. There was slowing of the pulse rate after delivery of the fetus in 72 per cent, no change in 22 per cent, and an increase in 6 per cent of the cases. The slowing occurred largely when the pressure rose.

Restlessness, noted in 5 per cent of the cases, was easily overcome by intravenous morphine administered after delivery.

Nausea and emesis occurred in 7 per cent of the cases. Most of these occurred in cases done under PT-19.

Inhalation anesthesia was necessary in 4 per cent of the cases because the extent of anesthesia was not sufficient or the block failed.

Two patients complained of transient headache on the operating table. One was due to a sudden elevation in blood pressure caused by a dose of Neosynephrine. No case developed respiratory difficulty or dyspnea. No fetal deaths occurred and the majority of the babies cried spontaneously and resuscitation was not necessary.

The postoperative complications and complaints of the patients were few and not serious. Backache, which occurred in 2 per cent of the cases, was mild and disappeared in four to five days. There were no postoperative respiratory complications.

Headaches occurred in 4 per cent of the cases. The usual analgesics were effective in controlling them. These were not considered the typical post-lumbar-puncture headache, inasmuch as they were not affected by postular changes. Urinary retention requiring catherization was present in 5 per cent of the cases. Catheterization was required once in all except one patient who was catheterized three times.

DISCUSSION

Obviously the chief hazard in spinal anesthesia for Cesarean section is the sudden, precipitous, severe hypotension encountered. The characteristics are the same as those seen in general surgery, namely, a comparatively marked reduction in systolic pressure, a slight reduction in diastolic and a reduced pulse pressure.

Severe as it was, the hypotension was overcome by vasopressor drugs, such as ephedrine and neosynephrine. Although the vasopressor may be administered prophylactically, it is preferable to administer it when needed and in the amounts required to produce the therapeutic effect. Prophylactically it is best administered intramuscularly and not subcutaneously, or, as is frequently done, in the interspinous ligament. It must be injected deep into the muscle tissue, long before the hypotension occurs, otherwise, it will not be absorbed. When the hypotension has ensued, the intravenous route is the only effective route.

Of particular interest is the elevation in blood pressure occurring immediately after the delivery of the fetus. As a rule, at the time of delivery of the baby, ergotrate and pitocin are administered. Whether or not this increase in blood pressure is due to the release of abdominal pressure with subsequent improvement of the venous return to the heart causing an increase in cardiac output, or to the administration of oxytoxics, is not easily answered. It is our feeling that the former explanation is more plausible. The rise does not occur in patients when inhalation anesthesia is employed, even though the same oxytoxics are administered. In some cases in which there was a delay of several minutes in giving the oxytoxics, the elevation in pressure appeared to coincide with the time of delivery. It is notable that there is a reduction in pulse rate with this elevation.

Fatalities from spinal anesthesia may be attributed to one of two causes: circulatory failure and respiratory failure. Respiratory failure results when the drug spreads along the thoracic and cervical roots in sufficient amounts to cause motor paralysis. The intercostal muscles and diaphragm are paralyzed and the patient dies from as-

phyxia. If recognized and immediately treated with artificial respiration until the effects of the drug "wear off", the outcome is favorable. Circulatory failure leads to a decrease in blood flow through the cerebrum, which is in turn followed by respiratory failure. Herein lies the answer to "What is the hazard of spinal anesthesia in Cesarean section?". From the foregoing cases, it is obvious that the degree of circulatory failure is quite pronounced, even in normal subjects free from circulatory complications. It comes on abruptly, is precipitous and fluctuates widely under the influence of vasopressors until delivery, at which time the blood pressure abruptly stabilizes. For some time it has been recognized that patients who have increased intra-abdominal pressure, such as seen when marked distention, large tumor masses or ascites are present, develop a serious degree of circulatory failure when spinal anesthesia is induced. Pregnant subjects respond in exactly the same manner. If one is not on hand to immediately institute therapy to combat this circulatory collapse the moment prodromal symptoms herald its approach, respiratory failure follows and the outcome is fatal. Patients who have been resuscitated and survived prolonged circulatory collapse have had permanent cerebral damage of varying degrees due to anoxia. In view of the suddenness and the severity of the circulatory depression, it is unwise for the obstetrician to attempt the dual role of operator and anesthetist. Another physician who is well acquainted with the physiological changes occurring during spinal anesthesia and who knows how to cope with them should stand by to devote his undivided attention to the patient during the early period of anesthesia. The fatalities reviewed all occurred when the operator assumed the aforementioned dual role. A vein should be cannulated, preferably before anesthesia is induced, to immediately introduce the vasopressor in the event it is needed. Fluids, though ineffective to overcome the hypotension, which is believed to be neurogenic, in origin may be needed later if there is hemorrhage or shock. Unless these requirements can be fulfilled, it is best to select another type of anesthesia. The obstetrician who is compelled, because of circumstances, to act as operator and anesthetist, had better avoid spinal anesthesia for Cesarean section.

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THE USE OF A HISTAMINE ANTAGONIST IN INTRAVENOUS PYELOGRAPHY

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The advent of the technic of intravenous urography has provided a distinct advantage in studies of the upper urinary tract. The procedure consists of an intravenous injection of a contrast medium for purposes of roentgenographic visualization of the urinary tract. Unfortunately, the performance of intravenous urography is not entirely devoid of danger which becomes manifest as sensitivity reactions of variable degrees of severity and even sudden death. In an effort to guard against these undesirable reactions, this study has been conducted for the purpose of observing the value of a histamine antagonist drug as a prophylaxis against the sensitivity reactions following intravenous pyelography.

"Diodrast" N.N.R. or iodopyracet injection (the diethanolamine salt of 3,5-diiodo-4-pyridone-N-acetic acid) is one of the most widely used drugs employed for intravenous urography. The solution is of 35 per cent concentration, the iodine content being approximately 49 per cent. Other contrast media utilized in the visualization of the urinary tract include "diodrast compound solution" N.N.R., "skiodan" N.N.R., "hip-

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puran" N.N.R., "iopax" and "neo-iopax" N.N.R. Although these drugs differ in respect to chemical configuration, all of these substances contain iodine[1].

The various reactions to these drugs are presently believed to be due either to their iodine content or some other substance which is formed as a result of the introduction of these drugs into the body. The immediate reactions are arbitrarily classified as mild, moderate, severe, and fatal. The mild reaction usually begins with a tickling sensation in the throat followed by nausea; flushing of the upper half of the body may occur simultaneously or soon afterwards. The moderate reaction sometimes consists of nausea and vomiting; not infrequently, sneezing and generalized itching followed by urticaria occur. The onset of the severe reaction may make its appearance with some or all of the preceding complaints. Edema of the eyelids and lacrimation may occur first followed by laryngospasm, respiratory difficulty, vertigo, syncope, cyanosis and shock. Fatal reactions can occur after the injection of only a single cubic centimeter of the drug or within a few minutes after completion of the intravenous injection.

The realization of the potential hazards of intravenous urography makes it imperative that patients, who are being considered for this type of diagnostic procedure, should be investigated for the presence of sensitivity to the contrast media. Particular importance should be given to patients who have a history of allergic bronchial asthma, hay fever, hives, drug allergy, and seasonal allergic manifestations.

There are also available several simple tests for the determination of the individual's sensitivity to these drugs. An oral test has been described by Dolan[2] in which 2 c. c. of the drug is placed under the tongue of the patient. If there has been no reaction at the end of ten minutes, the patient is instructed to swallow the solution. If no reaction occurs at the end of thirty minutes, the test is regarded as negative. A positive reaction consists of a perioral numbness followed by a "funny feeling" in the tongue which soon begins to feel thick and swollen and may even give the sensation of filling the entire mouth. A reliable and more rapid test has been described by Archer and Harris[3] in which one drop of the drug is placed in the conjunctiva of one eye. Three to five minutes later, both eyes are examined. The occurrence of conjunctival irritation in the tested eye as compared to the control constitutes a positive reaction. An excellent test, which was introduced by Naterman[4] and modified by others, consists of the intradermal injection of 0.05-0.1 c. c. of the drug with a control intradermal test below it. The sites are examined three to five minutes later. A positive reaction consists of the appearance of a wheal or area of erythema of about 1.5 cm. in diameter about the point of injection of the contrast agent.

The necessity for taking adequate precautions against these reactions has been emphasized in the medical literature many times. In a recent excellent report by Alyea and Haines[5], 1,675 patients were studied for possible anaphylactic reactions who had previously received the intradermal test for sensitivity to "diodrast". The incidence of general reactions in this series was four times as high in patients who had positive intradermal tests as in those with negative cutaneous reactions. In their group of patients with allergic histories (i.e., bronchial asthma, drug sensitivity, etc.), the incidence of general reactions was 70 per cent in those patients with positive skin tests as contrasted with 13.6 per cent in those with negative intradermal test findings.

This is a report of the clinical experience with the use of a histamine antagonist in the preparation for intravenous pyelography of 22 patients, all of whom presented histories of allergic manifestations of one or more types. Each of these patients had positive conjunctiva and intradermal tests for sensitivity to "diodrast". The control group consists of 50 patients, all of whom had non-allergic histories and had negative

conjunctiva and intradermal sensitivity tests to "diodrast".

The rationale of using a histamine antagonist in this study was based on the encouraging reports of clinicians in the treatment and prevention of numerous allergic conditions. In view of the belief that the reactions following the intravenous injection of contrast media for intravenous pyelography is due to allergic phenomena, the use of a histamine antagonist was deemed worthy of a trial.

The routine employed in the preparation of these patients for intravenous urography is as follows:

1. On the day prior to the urographic study, a history of any of the clinical allergic manifestations is obtained. Conjunctiva and intradermal skin tests for sensitivity to "diodrast" are performed.

2. Nothing by mouth after the evening meal until the urographic studies are completed the following morning. (EXCEPTION: Par. 4.)

3. Purgation with castor oil at bedtime.

4. One hour before the pyelograms are to be made, the patient is given 50-100 mgm. (depending on size and age) of "pyribenzamine" (N,N-Dimethyl-N'-benzyl-N' (a l p h a-pyridyl) ethylenediamine monohydrochloride (Tripelennamine). This drug is taken by mouth with one-half glass of water.

5. The contrast medium is injected intravenously in the following manner. One cubic centimeter is injected very slowly with a tuberculin syringe. Wait five minutes. If there is no reaction, complete the injection slowly with a constant eye on the patient. The appearance of any allergic manifestations is a signal for immediate discontinuation of the injection and the administration of epinephrine or ephedrine. The patient is observed thereafter until all evidence of danger has apparently disappeared.

The exclusive use of "pyribenzamine" in this series was not based on the belief that this drug is the best of the available histamine antagonists. The drug was employed early in this investigation and its use was continued for the sake of being consistent.

The results obtained with the routine described above were as follows. No allergic reaction occurred in the control group. The incidence of allergic reactions to the intravenous injection of "diodrast" and the other contrast media is about 4 per cent in those patients who are non-allergic both in respect to history and sensitivity tests. Although it is possible that the histamine antagonist could have been an important contributing factor to the absence of allergic reactions in these patients, no definite conclusions can be fairly deduced from the findings of such a small series as comprised the control group in this study.

Of the patients in the allergic group in respect to history and sensitivity tests, 4 patients, or 18.2 per cent, developed general sensitivity reactions. One of these 4 patients began to vomit after the intravenous injection of 0.5 c. c. of the drug. Another patient became flushed about the head and neck and developed intolerable itching after 12 c. c. of the drug was injected. The injections were discontinued in both of these cases. The other 2 patients developed urticaria and itching almost immediately following the completion of the injections. All of the patients responded well to adrenalin, 5 minims, by hypodermic injections; 100 mgm. of "pyribenzamine" was administered orally as soon as the patient was made comfortable. There were no fatalities.

CONCLUSIONS

A histamine antagonist was utilized in the preparation of patients for intravenous pyelography. The appreciable diminution in sensitivity reactions in those patients who possess various allergic disorders and manifest positive reactions to the sensitivity tests to the contrast media justifies continued use of this technic.

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CORNEAL TRANSPLANTATION*

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KERATOPLASTY

The history of keratoplasty which had its beginning in 1789 when Pellier first attempted the construction of an artificial cornea made out of glass with a supporting ring of silver is replete with interesting experiments and observations up to the present time. Some of the highlights of this era should be mentioned.

1. Reisinger—1818—transplanted cornea to replace opaque cornea. The idea originated with Himby who suggested it in 1813. Reisinger in his paper in 1824, the first of its kind to appear in print, also named the operation keratoplasty.

2. Thane—1834—total corneal transplantation.

3. Stilling—1836—suggested using only a piece of the cornea corresponding in size to the pupil.

4. Koenigshoefer—1840—first to suggest double-bladed knife; used two Beers knives joined together; also the first to use cadaver transplant.

5. Markus—1841—first to formulate the conditions necessary for a successful operation: (1) exact fit as to size and shape of transplant, (2) speedy transportation of the transplant from donor to host, (3) avoidance of the crytalline lens and the vitreous humor, (4) fixation of the transplant. Used gold clips to fix transplant in place of sutures.

6. Steinberg—1843—devised a trephine-shaped instrument 8 mm in diameter.

7. Desmarres—1843—mentioned possibilities of heteroplasty; felt that hosts's cornea gradually replaced the donor graft.

8. Malhagn — 1845 — first to suggest keratectomy.

9. Nussbaum — 1856 — insertion of a crystal-shaped stud into leucoma which had first been incised.

10. Pilitz—1859—tried using glass in place of corneal tissue.

11. von Hippel—1877—trephine—used both penetrating and non-penetrating methods; got his best results in non-penetrating grafts.

12. Zirm—1905—brilliant result in one case brought about a renewed interest in the subject; used a partial penetrating method in a man with bilateral leucomata as a result of lime burn. Vision of 0.1 was obtained in one eye, the other eye was lost from glaucoma. A five year follow-up was kept on this patient.

13. Plange—1908—Auto-transplant.

14. Elsching — 1908-1930 — 203 operations performed with an average of 73 per cent takes; 20 per cent had excellent visual results.

SELECTION OF CASES FOR CORNEAL TRANSPLANTATION

No general rule may be applied for the selection of cases favorable for corneal transplantation. Each case must be dealt with individually, and a general appraisal made. In studying the patient's eye condition, the following factors must be taken into consideration.

Environmental Factors—What are the indications and need for the operation? A patient with reduced vision as a result of a scarred cornea and who is well adjusted to his environment and is self-supporting, might better be left alone, even though the corrected vision is below 20/200. This is especially true if the eye falls into that group of cases which is designated as doubtful for the improvement of vision. This group of cases will be dealt with in more detail later on. The ophthalmologist should be especially guarded in giving advice to one-eyed patients.

The physical condition and age of the patient is an important factor, as in other types of intraocular surgery. This exami-

*Read before the Eleventh Annual Meeting of the New Orleans Graduate Medical Assembly, New Orleans, February 26, 1948.

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nation should include a medical survey such as is usual preliminary to cataract operations. Some knowledge of the patient's psychological make-up should also be known. Highly nervous and poorly emotionally adjusted persons make especially poor candidates for this type of ocular surgery.

Age Group—Another important factor to remember is that corneal grafting cases belong to a much lower age group than do cataract patients. A failure following a cataract operation does not lead to quite as serious consequences from an emotional and economic point of view. Most cataract patients have reached the retiring age and do not look forward to a very active life. Successful operations have been performed on babies as well as people in their seventies and eighties. Transplantation in the very young is to be avoided because of the difficulty in dressing and the greater danger of infections. Dressings have to be done under general anesthesia, and the danger from sudden and violent movement during the early post-operative stages might possibly cause a dislodgment of the graft from its bed.

Unfortunate newspaper dramatization of this type of surgery makes it more difficult for the surgeon in many instances to select proper cases for operation. Great pressure is often brought to bear on the surgeon by the patient's family and interested groups or individuals to do something, when the surgeon's better judgment tells him not to. Many patients travel great distances in the vain hope of being operated upon, when their local doctor could have prevented useless expense.

Iridectomy—No case of scarred cornea should be operated upon if an iridectomy would bring about an improvement in vision. Just how much improvement in vision should be obtained by an iridectomy must be left up to the patient to decide. The greater risk of performing a corneal transplanting operation should be explained to him. Before making this decision it is well to see how much improvement in vision may be obtained by dilating the pupil. If there is material improvement in vision, there can be no question that an optical iridectomy should be performed. In doubtful cases there is no disadvantage in first doing an iridectomy. If there is no improvement in sight, a transplant may be performed subsequently. If the cornea is so densely scarred that the pupil cannot be seen, transillumination should always be done, and an accurate idea obtained as to the size and shape of the pupil.

CLASSIFICATION OF CASES FOR OPERATION

1. Favorable for improvement of vision.
2. Partially favorable for improvement of vision.
3. Unfavorable for improvement of vision.
4. For cosmetic improvement.
5. For treatment of descemetocele.
6. Where preliminary surgery or treatment is necessary before final opinion may be given.

The most favorable cases are those in which there is a nebulous type of opacity, quite central, and in an otherwise normal eye. There must be no active corneal disease present, or active infection, of the conjunctiva, sclera, or uveal tract. There must be no increased intraocular tension, and no vascularization of the cornea. Blood staining of the cornea and conical cornea are usually favorable cases.

Conical Cornea—A very definite policy in the selection of conical cornea cases should be followed. At our clinic no patient is operated upon if the visual improvement with correction is better than 20/200 in either one or both eyes. This also includes those cases in which vision can only be improved by means of a contact glass. An exception is made in those patients that do not tolerate the wearing of contact lenses, in whom there has been a rapid deterioration of vision due to the development of central corneal opacities. It would seem more advisable to operate on these patients early and do as large a graft as seems feasible. It is interesting to note that the contact glass, if necessary for the improvement of vision, though not well tolerated before

the operation, may usually be worn with comfort after operation.

Partially favorable cases include those in which there is some corneal vascularization present such as in old cases of interstitial keratitis, and where the opacity, though central, is not too dense, and with only a small amount of clear cornea surrounding it.

Cases of adherent leucoma do not do well as a rule, unless the adhesions are first destroyed by a preliminary operation or irradiation. Extreme shallowness of the anterior chamber adds little to the technical difficulties of the operation, though there may be greater danger of anterior synechiae forming after the operation.

The diagnosis of glaucoma in the presence of kerectasia or keratoconus is most difficult to make. Its presence should always be suspected. A Baillart type of tenometer may be helpful, as with this instrument the degree of scleral rather than corneal indentation is measured. If there is any doubt concerning the diagnosis of glaucoma, an attempt should first be made to lower the intraocular tension by one of the filtering types of operation.

Corneal Dystrophy—Most cases of corneal dystrophy are not favorable for corneal transplantation. This is especially true of the Fuchs' endothelial and epithelial types of dystrophy. From present knowledge it would appear advisable to operate early in the course of the disease when the opacification of the cornea is not too dense and does not include all the layers of the cornea. Salzmann's[1] corneal dystrophy usually has some blood vessels present, but if these vessels can first be destroyed by irradiation, the transplant should be attempted on one eye, if the other eye has useful vision. Groenouw's[2] dystrophy appears to give a more favorable result. Here again it is a question of degree and density of the opacification of the cornea. Some cases of fatty or lipoid degeneration of the cornea may be favorable for operation. Calcareous degeneration, if it involves the entire cornea and the full thickness of the cornea, should not be operated upon. However, if the degeneration is band-shaped and not too dense, with some clear corneal tissue surrounding the scarred area, corneal transplantation should be performed.

Unfavorable for improvement of vision are cases with marked nystagmus as these eyes are amblyopic, and though a clear graft may be obtained, the visual results are disappointing. Densely scarred corneas from powder burns do poorly following transplantation. The same applies to lime burns of the cornea, but only if all the layers of the cornea are involved. Any eye which is hypersensitive to light trauma such as measurement of intraocular tension should not be operated upon until the cause of the hypersensitivity is discovered. Little experience has been had in operating on old trachomatous eyes, but the general principles laid down concerning degree of vascularization and opacification would hold in the selection of these cases for operation.

For Cosmetic Improvement—Many cases where tattooing was formerly resorted to in order to hide a disfiguring scar might be improved by corneal transplantation. In some few cases an improvement of vision may be obtained though this is not the general rule, due to many complicating factors. In general, tattooing and corneal transplantation do badly in the presence of a highly vascularized cornea.

For Treatment of Descemetocele—There is perhaps no more favorable treatment of this condition than corneal transplantation. Cauterization and repeated paracentesis are usually palliative measures. Conjunctival flaps only add to the disfigurement of the patient's eye, and often the flap becomes incarcerated in the wound. Transplantation should not however be attempted if there is a markedly increased tension, or in the presence of large corneal blood vessels. The degree of vascularization should be one of the most important and determining factors.

Where there is extensive vascularization of the cornea preliminary radiation (Iliff)[3] should be performed, and unless all the larger vessels are completely destroyed, keratoplasty is bound to meet with failure.

It is true, however, that in a few cases where smaller blood vessels have been present before operation, after the transplant operation has been done, the vessels will grow to the edge of the graft and tend to extend along the scarred area without actually penetrating into the graft itself. Apparently the scarred tissue formed in the cornea following a transplant operation will act as a barrier in some cases, but it is not wise for the surgeon to depend on this as there is no way of predicting whether the vessels will penetrate into the graft or not.

It is not always necessary to do preliminary surgery for anterior synechiae if they are small and of delicate structure, as these can be attended to at the time of operation. It is poor surgical judgment to operate on any eye in which there is an active uveitis present, but it is an interesting fact that several have been operated upon and that immediately after the operation a recurrence of a previously active uveitis was noticed with large KP deposits noted on the posterior surface of the graft. All these patients made uneventful recovery and the KP deposits have since disappeared. One has been followed for a period of three years with no recurrence of the uveitis, and the transplant has remained clear.

Therapeutic Keratoplasty—I have had no experience with therapeutic keratoplasty but many references have appeared in literature. Feldman[4], Shartz[5], and Filatov[6] advocate a partial penetrating keratoplasty for such conditions as serpent ulcer and tubercular interstitial keratitis. It does not appear to me, however, that this form of treatment is advisable. Inactive cases of interstitial keratitis do well in the absence of large corneal blood vessels.

Partial Non-penetrating Keratoplasty—Very little has appeared in English literature concerning partial non-penetrating keratoplasty but from foreign reports it would appear that the results of this method are nearly as good as results from a penetrating type of keratoplasty. It may be that this method may eliminate the need for keratectomy in many instances. It is not the purpose of this presentation to discuss this subject.

OPERATIVE TECHNIQUE

After more than ten years' experience in doing corneal transplantation, during which time several hundred cases have been operated upon, the following observations may be of some interest. Partial penetrating keratoplasty may be performed by the use of:

a) Stencils to outline the window,

b) A double-bladed knife as first suggested by Koenigshoefer in 1840, or

c) The trephine method as originally suggested by Steinberg in 1843.

The trephine method offers several advantages over the square window:

1) Better cosmetic result.

2) Outline of window made easier because of adjustable stop on trephine.

3) Adjustable stop also prevents trephine from becoming dulled during sterilization.

4) Donor window is cut through completely with trephine, eliminating use of scissors and unnecessary manipulation of donor graft.

5) Specially curved scissors used to complete cutting of window in host's eye more easily manipulated than the straight scissors used in the square graft.

The steps in the operation:

a) *Donor eye*—the eye is brought to the operating room from the Eye Bank in a moist chamber. The Eye Bank only sends eyes which have been carefully selected for this type of operation. If there is any question about the condition of the eye, especially the condition of the cornea, this report is given the surgeon before the operation. The age, sex, color, cause of death, etc. of the donor must always be reported to the surgeon operating. He has the final choice of whether the donor cornea is in good condition and on his shoulders rests the responsibility of the outcome of the operation. Eyes of still-born are unfavorable as the tissues are too malleable and delicate and there appears to be more edema of the graft following operation. The upper age limit is not exactly known, as the

eyes of people in their sixties have been used with favorable results. Gliomatous eyes should not be used as there may be a deposit of cells on the posterior surface of the cornea. Eyes with tumors may be used if the tumor is confined to the posterior segment. As a general rule, glaucomatous eyes are not favorable donor material as there is frequently a bedewing and edema of the endothelial surface. Any eye with intraocular infection should not be used even though the cornea may clear.

b) *The graft* may first be cut from the donor eye while the assistant prepares the patient as for a cataract operation. The donor eye is removed from the sterile glass moist chamber and held in one hand, using a piece of gauze wrapped about the eye to keep it from slipping while the window is being cut. The trephine must be exceedingly sharp and should have been previously tested by the surgeon before giving it to the operating room nurse for sterilization. The surgeon holds the donor eye in one hand, places the cutting edge of the trephine on the cornea, being careful to get it exactly centered, and with several quick rotations of the trephine cuts a complete window. To assure rapid and complete penetration, slight pressure should be put on the donor eye with the fingers of the other hand. As the trephine is rotated, the surgeon makes sure of complete penetration throughout the 360° of the arc, even at the risk of destroying the iris and lens of the donor eye. Very frequently the donor window impinges on the inside of the trephine and considerable manipulation may be necessary to dislodge it. With the use of a stilette or plunger made to fit the inside bore diameter of the trephine, the cut window may be dislodged without injury to its endothelial surface. The window when removed is placed on a fenestrated spatula, endothelial surface uppermost, and set aside while the recipient's eye is prepared. It has not been thought advisable to place the donor window in saline solution, but preferably in a moist chamber as the saline tends to produce edema of the graft, and perhaps lead to certain complications later on.

c) *Preparation of the recipient's eye*—After the usual pre-operative preparation, sedation, lid block, etc., a retrobulbar injection may be given if the intra-ocular tension is elevated. As a general rule, it is easier not to operate on too soft an eye. The trephine does not bite into the corneal tissue as readily, and considerable pressure must be exerted by the surgeon before penetration is obtained. Since the development of a trephine with an adjustable guard, this danger is not quite as great, but the facts mentioned should be kept in mind.

d) When a sufficient depth on anesthesia has been obtained, the window is outlined using the same trephine that was used in obtaining the donor window, but the guard, instead of being set at any depth over 2 mm. is now set at a depth of ½ mm. or less. This is done in order to prevent penetration into the anterior chamber before sutures have been properly placed in position.

e) Fluorescine is dropped on the cornea to further accentuate the outline of the window.

f) Two figure-of-eight sutures D&G 7-0, one black and one white, are placed in position. Each bite should be taken close to the outlined window as possible, the average distance being about 1 mm. The needles should not perforate more than the anterior third of the cornea and the bite should not be over 3 mm. in length with each suture employed.

g) A central traction suture is next placed through the superficial layers and tied, and the ends cut short.

h) Cutting of the window is completed after the sutures have been laid aside. The exact amount of penetration is judged by a movement of the iris, or a sudden gush of aqueous fluid. If observation of these two factors are remembered, it is rare indeed that injury to the iris or lens occurs. It is too hazardous to attempt cutting a complete window with a trephine as has been

suggested when using the Green automatic trephine.

i) Once perforation has been made along one border, specially made curved scissors are used to complete cutting the window. To facilitate this procedure the previously placed central suture may be grasped with iris forceps and traction made at the point where needed. In cutting the window, even though the scissors have the exact radius of curvature of the trephine, an attempt should be made to cut slightly beyond the outline made. This allows for the thickness of the jaws of the scissors and leads to a more perfect fit.

j) Atropine 3 per cent is instilled through the open window when the button has been completely excised. The previously prepared donor graft is placed in position and the sutures securely tied.

Post-operative Care—The first dressing is performed forty-eight hours after operation. Atropine and Metaphen 1:2500 aqueous solution are employed. Daily dressings after that. The pupil is kept well dilated with mydriatic, and penicillin ointment is used after the first dressing in place of Metaphen drops. Sutures are removed on the tenth day, or later, depending on whether suture is cutting into graft or whether there is a beginning stitch abscess. If anterior synechiae develop, these should be treated before the patient leaves the hospital in most instances.

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DITHIOPROPANOL (BAL) IN THE TREATMENT OF BICHLORIDE POISONING

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Since the American and British governments have released information on BAL British Anti-Lewisite) (dithiopropanol), its efficacy in the treatment of arsenical poisoning has become well known. Recently, I had the opportunity to observe its effects in bichloride of mercury poisoning. That one case is no basis for a conclusive report is realized; however, this case is intended to signal out the possible use of the drug in the treatment of a heavy metal poisoning other than arsenic.

It will be of interest to review what occurs when bichloride of mercury is ingested. It is most injurious when ingested completely dissolved on an empty stomach. When swallowed in tablet form, it is least harmful, for the tablet is rushed along the intestinal tract at a rapid rate and absorption is slow.

The bichloride of mercury passes into the blood stream and is deposited in the various organs, ultimately in the kidneys where the greater part of the damage is done to the tubules. These structures show signs of degeneration and obstruction. A tubular type of nephritis develops and the result is the failure to excrete urine, which means the retention of nitrogenous waste and excessive water.

It is known that not all units of the kidneys function simultaneously, and each day some percentage of them comes into play. The number that are called upon may well be in proportion to that particular moment's need. For instance, if the nitrogenous waste is excessive, more units may be called upon to keep the non-protein nitrogen at a constant. Therefore, at the time the poison is ingested, only those tubules functioning are damaged, but as the poison is being picked up by the blood stream and presented to the kidneys for excretion, there results a continuous stream of tubular pathology. If something should be done early to neutralize the bichloride of mercury in the tissues and blood stream, then the tubular damage would cease. If the neutralizer were given immediately after ingestion, very little damage of the kidneys should result. However, if the poison is not combatted early, it is evident that the kidney damage will increase progressively

each day. With the increase of waste products, the body calls upon a greater number of units to function, thus rapidly eradicating the kidney units.

CASE REPORT

A white female, aged 24, ingested ten capsules of nembutal (15 grains). On an empty stomach, the following day, she took two tablets (7½ grains each) of bichloride of mercury dissolved in a glass of water. Due to severe pain along the upper digestive tract, she was forced to call for assistance; the number of hours lapsing between the administration of the drug and the arrival of assistance is not known. She was admitted to a hospital. By means of gastric tube, egg albumin and milk were introduced into the stomach. The patient began to vomit; none of the blue coloring was seen. Six hours after admission, the vomitus contained blood and necrotic material. With each attack of vomiting, there was a bowel movement, blood frequently appearing in the stool. Continuous type of vomiting persisted for about 36 hours, during which time she was given two liters of normal saline intravenously. In spite of receiving no fluids by mouth, she would bring up from 200 to 300 c.c. of fluid with each vomiting seizure. When the vomiting showed signs of subsiding, she was given 5 per cent glucose in distilled water, which had to be discontinued when evidence of edema of the face and neck appeared.

On the second day, the patient had violent attacks of hiccoughs, and there was pain upon swallowing. Thereafter, the mouth and throat were a constant source of pain. The mucous membrane of the gums showed signs of large areas of erosion. The gums were bleeding and presented deposits of mercury. On the fourth day, the patient was given an infusion of 5 per cent glucose in distilled water. Immediately thereafter, she began to have tachycardia and difficulty on respiration, drowsiness and blurred vision. Her general condition was bad. During these four days, she did not void. One-half ounce of urine was obtained by catheter on the fourth day. The patient was then wrapped in rubber sheets, about which were placed hot, wet blankets and hot water blankets for 30 minutes. During this time, she perspired profusely and her condition improved for a few hours. The next morning BAL was obtained and she received 1.2 c.c. intramuscularly and four hours later, a similar dose. Her condition began to improve and she felt better; the mental cloudiness was lost and she no longer heard voices. The mouth soreness improved and vomiting and diarrhea subsided to one or two attacks per day. She began to void within a few hours one-half ounce amounts at frequent intervals. She was able to retain water and soft drinks. The edema about the face began to subside. The BAL was given every four hours for six doses. Fifteen to 20 minutes after the third and successive doses of BAL, she experienced burning of all the membranous surfaces of the body, nausea with profuse salivation and a sensation of constriction of the chest, all of which lasted not more than 30 minutes. The amount required to produce these symptoms was smaller with each consecutive dose. This patient finally became uncomfortable with 0.5 c.c. dose. After the six consecutive doses at four hour intervals, she was given one daily for two days. By the third day of administering BAL, she was voiding an ounce or more every few hours. Prior to her discharge from the hospital, her NPN rose to 225 mg. and creatinin to 13.9 mg. per cent. She was discharged from the hospital three days after the BAL was administered and seven days after admission. Four weeks after being hospitalized, her NPN was 35, creatinin was 1.5 mg. per cent and PSP was 60 per cent.

DISCUSSION

This patient had ingested bichloride of mercury in its most lethal preparation. She developed an acute anuria that lasted three days, the NPN rose to 225 on the third day, the creatinin to 13.9. She had an encephalitis apparently due to mercury poisoning, also a myocarditis as demonstrated by a pulse irregular in rhythm and force and accompanied by a precordial heaving. All of these findings disappeared with the administration of BAL. Although the chemistry was the same, the patient had a sense of well being and mental clarity; the voices she had heard had disappeared. The soreness of the mouth and throat improved. The deposits of mercury along the gum edges and the bleeding of the gums subsided. The vomitus showed less clotted blood and other necrotic materials. The bowel movements became normal on the second day of treatment.

It appears that the administration of fluids in these patients should be guarded with every factor of safety. In the beginning, when the vomiting was frequent, the replacement of fluid and chlorides was indicated for this patient, but when it stopped and the patient was retaining fluids, they would, if pushed, have definitely killed her. The heart was already toxic and the throwing on of an extra load would have been dangerous. The presence of an excessive amount of fluids in the tissues is sufficient stimulus for the kidneys to rid the body of this accumulation. The fact that these in-

dividuals who recover have good to excellent kidney function indicated that only a small number of the functioning units are destroyed. Because of the response to BAL in this case, it would seem that if this patient had received BAL on admission instead of the fourth day, she would have given little cause for anxiety.

Due to the gravity of the patient's condition, dental hygeine was neglected and she developed a serious Vincent's angina. In all cases of this kind, a dentist should be consulted as soon as oral complications appear so as to prevent permanent dental damage.

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NITROGEN MUSTARD THERAPY*

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The chemistry, biological actions, and history of the nitrogen and sulphur mustards have been amply discussed in an article by Gilman and Philips in Science of April 1946. The nitrogen and sulphur mustards owe their physiological activity to a chemical reaction which takes place when they are put in aqueous solution. Under these circumstances an intramolecular cyclization occurs with the formation of an active cation, ethylenimonium in the case of the B-chloroethyl amines. The ethylenimonium ion has great affinity for many functional groups of compounds of biological importance, such as the sulphide, phenolic, and E-amino groups of amino acids and peptides.

The ability to cause the death of cells is the outstanding property of the nitrogen mustards. It is not known just how this action takes place, but it is thought that inactivation of enzyme systems with the production of irreversible metabolic defects in the cells may be the mode of action. Another explanation is that the drugs are specifically nucleotoxic. Susceptibility of cells to the action of the nitrogen mustards is directly related to the degree of proliferative activity; hence, tumor cells, lymphatic tissue, bone marrow, and gastrointestinal mucosa are especially susceptible. When these halogenated alkylamines are given in large doses to experimental animals, the normal tissues mentioned and transplanted tumors show evidence of the marked destructive activity of the drugs. Complete aplasia of the bone marrow may be produced in this manner. The biological effects of the nitrogen mustards resemble in many ways those of roentgen rays. Indeed, it has been suggested by Hardin B. Jones, in the American Journal of Roentgenology and Radium Therapy of July, 1947, "that perhaps the neoplastic inhibiting mechanism associated with tissue irradiation is a chemical substance and is not due to tissue ionization directly." It has been shown that a number of the delayed effects of irradiation can be duplicated by toxic chemicals as, for example, the anemia in benzol poisoning.

As a general statement, it may be said that nitrogen mustard therapy has not proved superior to the x-ray in the treatment of lymphomas and leukemias. Its optimal therapeutic benefits have been observed in Hodgkin's disease. It has been suggested that nitrogen mustards be used to treat patients with lymphomas that have become radio-resistant, as a response can be anticipated in a large number of these patients. It has been observed that cases which have become resistant to roentgen therapy may, after a course of methyl bis B-chloroethyl amine, again become radiosensitive. The exact importance of the nitrogen mustards and their relation to radioactive substances and x-rays is not yet fully determined.

DOSAGE AND MODE OF USE

An optimum therapeutic dose of (methyl bis) nitrogen mustard has been tentatively established as being .1 mg./kg. of body weight. Four such doses constitute the average course of treatment. These are given usually, but not necessarily, on consecutive days. In carefully selected cases the calculated daily dose has been given for

*Read at meeting of the Orleans Parish Medical Society, December 8, 1947.

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as many as six to eight days. The drug is given by the intravenous route only. Nitrogen mustard is supplied by Merck & Co. in sealed bottles, each containing 10 mg. of the crystalline product. This is diluted with 10 cc. of normal saline, the proper dose withdrawn, and injected without delay into the tubing of a freely flowing saline infusion. The activity of the compound is rapidly dissipated after it has been dissolved. The injection may be made as rapidly as desired. We have noted no immediate reactions during administration of the drug; phlebothrombosis was encountered once at the site of injection. Patients receiving initial treatment should be hospitalized for the four days of therapy. Repeat doses, as reported by Jacobson, Spurr *et al.* in Medical Clinics of North America, January, 1947, may be given as an out-patient procedure.

Subsequent courses of treatment may be considered when the patient has recovered from the delayed toxic manifestation of the preceding treatment, particularly the hematopoietic depression. The time factor involved varies considerably and may be from two weeks to two months.

TOXICITY

The skin and eyes can be damaged by contact with the nitrogen mustards. Precautions should be taken to avoid any possible exposure. Local tissue necrosis may occur if the injection extravasates. Thrombophlebitis may develop at the site of injection, but this complication practically never occurs if the technique of administration previously described is used. Nausea and vomiting frequently follow each dose of the drug within a period of thirty minutes to three hours. A long-acting barbiturate given prior to the injection decreases the severity of these symptoms. Some of our patients experienced vomiting only with the first dose of the drug; one patient did not vomit at all. Anorexia develops in many of the patients, but disappears in one or two days.

The most important toxic action which confronts the clinician is the depression of the blood forming organs which occurs in all cases. However, an adequate clinical response can be obtained without affecting the formed elements of the blood seriously, if care is taken with the dosage. Lymphopenia is a characteristic reaction to the therapeutic exhibition of methyl bis (B-chloroethyl) amine. This develops within the first two days following treatment, and generally begins to subside during the second week. A granulocytopenia develops in the third week, generally persisting for about one week. There is a variable degree of thrombocytopenia during the first three weeks. Petechiae have been noted only occasionally. Mild reduction in the erythrocyte count is also observed, reaching its peak in about three weeks, but frequently a preëxisting anemia will improve as a result of the effect of the nitrogen mustards on the disease process. The chronological sequence of the changes in the peripheral blood parallels closely the changes which occur in the bone marrow. Repeated laboratory tests on the urine, renal function, hepatic function and blood chemistries have not revealed any toxic action; patients with known kidney and liver damage have been treated with repeated courses of nitrogen mustards without evidence of further impairment of function. It is interesting to note that infection rarely complicates the granulocytopenia observed in nitrogen mustard therapy.

DISEASES TREATED AND POSSIBLE VALUE

Since the first reported clinical use of the nitrogen mustards by Gilman, Goodman and others in Science, April, 1946, numerous reports have appeared on the use of these drugs in the treatment of neoplastic diseases. It seems to be generally agreed that the best results have been obtained in the treatment of Hodgkin's disease.

We will attempt to give a brief and tentative evaluation of the nitrogen mustards in the therapy of the lymphomas, leukemias, and allied disorders. Impressions of the therapeutic value of these drugs in a variety of neoplasms will be mentioned. These impressions are derived principally from a recent preliminary report of the National Research Council.

Hodgkin's Disease. A palliative response to nitrogen mustard is the rule in Hodgkin's

disease. The therapeutic effects noted are: marked diminution in the size of enlarged nodes, both peripheral and mediastinal, frequent decrease in the size of an enlarged liver or spleen, and a normal temperature in those patients exhibiting fever as a sign of the disease. An improvement in the appetite is consistently noted and feeling of well-being of the patient. The expected duration of remission after a course of therapy varies from one to five months. Remissions have been produced for as long as four years by treatment given at intervals of one to two months. Remissions thus effected appear to become of shorter duration with successive courses of the drug. At the date of writing no definite conclusion has been reached as to the comparative values of nitrogen mustards and irradiation in the treatment of Hodgkin's disease.

Lymphosarcoma. Beneficial effects of nitrogen mustard therapy are seen in lymphosarcoma but objective and constant features of the response are much less striking than are noted in Hodgkin's disease. The rapidity of response to treatment varies greatly. Duration of remission varies from none to eight months. In a case reported by Jacobson, Spurr *et al* in the J.A.M.A. of October 5, 1947, clinical remissions lasting up to eighteen months were noted. Therapeutic benefits are qualitatively similar to those seen in Hodgkin's disease. Remissions have been produced for as long as thirty-six months in 2 patients.

Polycythemia Vera. A few cases of polycythemia vera have been reported. The response to treatment has been favorable with clinical remissions lasting from three to seventeen months. More experience with the use of the nitrogen mustards in this disease will be necessary before a comparison can be made with other methods of treatment.

Chronic Myelogenous and Chronic Lymphatic Leukemia. Response to nitrogen mustard therapy in these conditions is noted mainly in a reduction of the white cell count, an increase in platelet count when thrombocytopenia exists, and frequently a reduction in size of an enlarged liver or spleen. Of the two conditions the response of patients with chronic lymphatic leukemia is more favorable. Therapeutic effects noted have been similar to the response seen in irradiation therapy of these diseases.

Acute Leukemias. There has been reported no evidence of therapeutic response in acute leukemias, and the use of the nitrogen mustards in these diseases is not encouraged.

Miscellaneous. Reports from investigators through the National Research Council indicate that nitrogen mustards have been used in cases of carcinoma of the lung, mycosis fungoides, multiple myeloma, head and neck tumors, carcinoma of the gastro-intestinal tract, carcinoma of the breast, carcinoma of the cervix and uterus, genito-urinary tumors, bone tumors, nervous system tumors, melanosarcoma, and miscellaneous conditions. There has been a wide variation in response of individual tumors within these groups. There have been no apparent cures reported to date. A palliative therapeutic response has generally been noted in mycosis fungoides, neuroblastoma, and to a lesser extent in carcinoma of the lung. Isolated and occasionally quite favorable responses have been noted in adenocarcinoma of the gastro-intestinal tract, embryonal tumors of the genito-urinary tract, fibrosarcoma, and carcinoma of the breast. It is suggested by the National Research Council that further clinical trials may be carried out on the use of the nitrogen mustards in the palliative treatment of metastatic malignant melanoma.

CASE REPORTS

We have treated 11 patients with the methyl-bis compound. The cardinal points of these cases are presented in table form (Table I). Detailed case reports have been forwarded to the National Research Council and will be used in the comprehensive study of the nitrogen mustards. Sixteen additional cases have been treated but the data is incomplete on these.

HISTOPATHOLOGICAL CHANGES NOTED IMMEDIATELY FOLLOWING TREATMENT

As stated previously, the effects of the nitrogen mustards on tissues are similar to

TABLE 1

SUMMARY OF 11 CASES TREATED WITH METHYL-BIS (B-CHLOROETHYLAMINE) HCl (NITROGEN MUSTARD)

PATIENT AND DISEASE	PREVIOUS TREATMENT	DURATION SYMPTOMS	IMMEDIATE THERAPEUTIC RESPONSE	FIRST REMISSION	IMMEDIATE TOXIC EFFECTS	MAXIMUM LEUKOPENIA	SUBSEQUENT TREATMENTS	(AV. DUR.) SUBSEQUENT REMISSIONS
No. 1, WF, age 43 Hodgkin's disease	X-ray, 1 course	6 mo.	Decrease size lymph nodes, felt well, afebrile	10 wks.	Nausea & vomiting, mod., all treatments	2,950	Two	2 mo.
No. 2, WM, age 33 Hodgkin's disease	None	3 mo.	Decrease size lymph nodes, liver, spleen; decrease temperature	12 wks.	Mild nausea & vomiting	1,500	One	2 mo.
No. 3, WM, age 52 Hodgkin's disease	X-ray, 1 course	6 mo.	Decrease size lymph nodes; symptomatic improvement	4 wks.	Slight nausea	2,000	One	In remission
No. 4, CF, age 37 Lymphosarcoma	None	1 mo.	Decrease size lymph nodes, liver, spleen; sympt. improvement	2 wks.	None	2,300	None	
No. 5, CM, age 12 Lymphosarcoma	None	1 mo.	None	None	Mod. nausea & vomiting	4,400	None	
No. 6, WF, age 59 Chr. m. leukemia	None	6½ mo.	Sympt. improvement. Reduction total WBC.	8 wks.	Mod. nausea & vomiting		Two	3 wks.
No. 7, CM, age 4 Lymphoblastic leukemia	None	9 days	Marked reduction in total WBC.	1 wk.	Mild nausea & vomiting	1,500	None	
No. 8, WM, age 2 Wilm's tumor	X-ray, Surgery	9 mo.	None	None	None	4,000	None	
No. 9, WF, age 58 Ca. of esophagus	None	4 mo.	None	None	Mod. nausea & vomiting	unrecorded	None	
No. 10, CF, age 25 Fibrosarcoma, metast. lung	None	11 mo.	Slight decrease in dyspnea	Treat. too recent to evaluate	Slight nausea & vomiting	None	None	
*No. 11, WF, age 21 Lymphoepithelioma metastatic	X-ray, Radium	2 mo.	Decrease liver size, sympt. improvement, decrease in fever	12 wks.	Nausea & vomiting, anorexia	3,000	Three	3 wks.

* See case report.

those of x-ray. The following study shows the similarity of the tissue response. Apparently the changes take place in a somewhat shorter period of time with the nitrogen mustards. The microscopic studies presented are from lymph nodes from a case of lymphosarcoma (case no. 4). Late histopathological changes have also been found to be similar to those seen in x-ray therapy.

Lymph Node before Therapy (2-15-47)	*Lymph Node after Therapy* (2-19-47)
Capsule—Thin, no invasion by tumor.	*Capsule*—Slight fibrous thickening with infiltration by tumor cells and lymphocytes in two areas.
Peripheral Sinus—Retained in areas, loose, filled with edema fluid, lymphocytes and few large mononuclear cells, some with 2 nuclei. Nonphagocytic.	*Peripheral Sinus*—Retained and appear dilated: contain numerous tumor cells, few lymphocytes. No evidence of mitotic division but no phagocytosis.
Architecture—All lymph follicles replaced by fairly large lymphoblastic cells (12-30 micra) in various stages of mitotic division with both typical and atypical multipolar mitoses. Essential cell contains large oval to rounded vesicular nucleus with prominent single to double nucleoli and very loose chromatin strands. Nuclear membrane distinct, cytoplasm scanty and basophilic with an ill-defined cytoplasmic membrane. No eosinophils. Fair number of mature lymphs present. No areas of necrosis. Reticulum stroma poorly defined. Intermediary sinuses replaced by tumor cells. Fair number small vessels present, lined by hyperplastic endothelium Evidence of phagocytosis meager.	*Architecture*—All lymph follicles replaced by larger tumor cells (18-40 micra) which appear to rest on a reticulum, have larger, more distinct cytoplasm with essentially the same type nucleus seen before treatment. Some of these cells are very large, up to approximately (60-80 micra), and contain eosinophilic, finely granular cytoplasmic masses, and some show phagocytosis of nuclear debris. Areas of necrosis, surrounded by these large cells with eosinophilic cytoplasm masses are seen in the region of primary lymph follicles. Some hemorrhage and dilatation of the sinusoids is apparent in these areas. Numerous bizarre mitoses are seen. No eosinophils present. Vessels appear more numerous and congested. Reticulum definitely increased.
	Note: Resembles node seen following irradiation.

A case of metastatic lymphoepithelioma is presented. The tumor was very sensitive to the action of the methyl-bis compound. A rather striking palliative response followed the first three courses of therapy. The patient's discomfort was relieved considerably by the antipyretic effect of the drug and the reduction in the size of the liver.

CASE REPORT (Case No. 11)

The patient is a twenty-one-year-old white female on whom a diagnosis of lymphoepithelioma of the nasopharynx, metastatic to cervical lymph nodes, was made by biopsy and microscopic study in November 1945. She was treated with roentgen therapy and radium needles with reduction of all masses. The last treatment was given in August 1946. There was no local recurrence of the tumor.

The patient remained asymptomatic until two months prior to admission in April 1947, when she developed high fever, weight loss, and anorexia. Examination revealed a pale, moderately emaciated, acutely ill patient; the temperature was 104°; the liver was palpable 8 cm. below the costal margin, firm, slightly tender and smooth. The spleen was not palpable. There was no enlargement of lymph nodes. The temperature rose daily to 104°-105°. Exhaustive studies for an infectious process were all negative. Biopsy of the liver revealed, on histopathological study, metastatic lymphoepithelioma to the liver. Hemogram showed 2,900,000 red blood cells; 31,350 white cells, 94.5 per cent neutrophils, monocytes 1 per cent, lymphocytes 4.5 per cent; 360,000 platelets. Serum proteins, icterus index, blood glucose and urea were within normal limits. Blood Kline and urinalysis were negative.

She was given 0.1 mg. of methyl-bis (B-chloroethylamine) HCl. per kg. of body weight for four consecutive days. A moderate degree of nausea and vomiting followed the first three doses. The temperature gradually returned to normal. The liver decreased in size and was palpable 5 or 6 cm. below the costal margin. She remained afebrile and developed a good appetite. A weight gain of 2 pounds occurred. She felt relatively well. Hemogram following treatment showed 3,500,000 red cells; 22,000 white cells, 85 per cent neutrophils, 15 per cent lymphocytes.

Twenty-six days after the first treatment a second course of nitrogen mustard was given, not because of recurrence of symptoms, but with the hope of giving her a longer remission.

Forty-three days after the initial treatment the liver was palpated 2 cm. below the costal margin. On August 1 the fever recurred and the liver was enlarged 5 cm. below the costal margin; it was very firm.

A third course of nitrogen mustard was given, approximately three months after the initial treatment. The liver became softer on palpation and the temperature approached normal. The white cell count was 8400 following treatment.

A fourth course of treatment was given in September, six weeks after the third course; at this time the liver had again become markedly enlarged. The fever was only of moderate degree, however. The hepatic size changed very slightly with this course of treatment. A leukopenia of 3000 was noted.

Because of the slight benefit derived from the

fourth treatment and because the patient's temperature remained at a relatively low level, no further treatment was given. She expired seven months after initial treatment.

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NEW ORLEANS
Medical and Surgical Journal

Established 1844

Published by the Louisiana State Medical Society under the jurisdiction of the following named Journal Committee:

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SUBSCRIPTION TERMS: $3.00 per year in advance, postage paid, for the United States; $3.50 per year for all foreign countries belonging to the Postal Union.

News material for publication should be received not later than the eighteenth of the month preceding publication. Orders for reprints must be sent in duplicate when returning galley proof.

Manuscripts should be addressed to the Editor, 1430 Tulane Ave., New Orleans, La.

THE JOURNAL *does not hold itself responsible for statements made by any contributor.*

FATAL AND NEAR FATAL REACTIONS FOLLOWING INTRAVENOUS MERCURIAL DIURETICS

Fatal and near-fatal reactions immediately following the intravenous injection of mercurial diuretics have been reported since 1931. Kaufman recently has collected 31 fatal cases and added one. Considering the wide use and value of these diuretics the matter is of much importance. The type of reaction under consideration is that which occurs during or within a few minutes of the injection. There are other reactions developing 6 to 12 hours after the injection which may be due to disturbance of the electrolyte balance, to allergy or to the usual type of mercurial poisoning.

The cause of the immediate reactions is considered to be the toxic effect of the mercurial product in the heart muscle. The more severely damaged the heart muscle the more likely possibility there is of acute symptoms. Various investigators have found in animals electrocardiographic evidence of damage to the heart muscle. Other observers were able to get electrocardiographic tracings on two patients from the time they received the mercurial diuretic intravenously until they died shortly afterwards. Both showed the development of ventricular fibrillation. Another, Ben-Asher reported "An electrocardiogram taken during the reaction showed changes in the P wave, ST segment and the T wave, followed by ventricular premature systoles and paroxysmal ventricular tachycardia. The patient recovered and the electrocardiogram returned to normal sinus rhythm."

The reaction follows the use of different mercurial preparations: Mercupurin, Salyrgan, Neptal, Esidrone, Mersalyl. The diagnoses in the fatal cases were congestive heart failure 16, nephritis 7, nephrotic stage of nephritis 4, nephrosis 4, unknown 1. Six deaths occurred with the first injection and the others after a variable number up to the 200th. It is to be observed that the patients in this series were not necessarily moribund, as many were ambulatory. The interval between injections did not appear to be significant. However the speed with which the injection was given was thought to be important. The development of symptoms is sudden and within one to three minutes after completion of the injection. The patients gasps, cyanosis and pallor appear, there is substernal distress, dyspnea and irregular respiration, convulsions are reported. Recovery is apparently dependent upon the ability of the heart muscle to withstand the toxic effect and seems relatively uninfluenced by supportive measures.

In study of the published reports various recommendations are given to avoid so distressing an occurrence. No fatalities have

been reported following intramuscular injections so this may be used when effective. As small doses given frequently are more effective than larger ones at longer intervals 1 c. c. is advised as the intravenous dose. The diuresis following such doses is increased by the previous administration of ammonium chloride. The injection should be given slowly at the rate of 0.1 c. c. every 15 seconds. Small amounts of magnesium sulfate (0.5 c. c. of 20 per cent solution) have been advised as an addition to the intravenous mercurial to prevent ventricular fibrillation. Also 500 mg. ascorbic acid have been recommended for this purpose.

It would appear from these reports that caution is needed in the use of the mercurial diuretics and that the risk, small though it is, can be materially diminished by attention to proper details.

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LEGISLATION AFFECTING PHYSICIANS

The Louisiana State Legislature has terminated its biannual session and many bills which concern the welfare of the physicians and the interest of the public in medical matters have been presented. Nowhere is it more conclusively shown than in certain proposed laws, that the public does not know its own interests. The dual role of the medical profession in treating disease and safeguarding the community health is clearly shown. The legislation committees of the Louisiana State Medical Society and the Orleans Parish Medical Society had a heavy responsibility here. In the last session and for years past they are to be congratulated on their care and patience in presenting the viewpoint of organized medicine and in showing that over a period of years the interests of the profession and of the public are the same.

The "chiropractor bill" is presented to each session and each time our representatives have to appear and again plead that those who practice medicine should be properly trained. Presented to the last session were four bills concerned with the regulation of practical nurses. Three were not desirable. The one which was best adapted to the interest of the community as a whole was supported and it is hoped it will become a law.

Proposed laws that would affect physicians and hospitals adversely were the source of concern to our committees. One such bill would have removed from a hospital the right to control admissions of professional staff. Another would have made obligatory the acceptance of any hospitalization policy. The physicians' point of view was adequately explained in these matters.

The forward-thinking and altruistic citizens of the community look to us to direct and influence the trend of medicine in the community interest. It is to be hoped that the efforts of the Legislative Committees of the State and Orleans Parish Medical Societies will continue to be effective as in the past and that in related fields of endeavor where the profession and the public deliberate in the community interest our good offices are equally valuable.

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ORGANIZATION SECTION

The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.

An informed profession should be a wise one.

EXECUTIVE COMMITTEE MEETING

The first meeting of the Executive Committee, under the presidency of Dr. M. D. Hargrove, was held in New Orleans on May 15.

1948 MEETING

At this meeting Dr. John G. Snelling, Chairman of the Committee on Arrangements for the 1948 meeting held in Monroe, presented report of his committee. It was

stated that the amount of one dollar per capita appropriated for entertainment for the meeting and the special appropriation of $1,000.00, approved by the Executive Committee, was not sufficient for handling of this meeting and the matter of finances for future meetings was discussed. It was decided that a special committee, from the Executive Committee, should be appointed to study this question.

1949 MEETING

The dates of May 5-7, 1949 have been approved for the next annual meeting to be held in New Orleans. Headquarters will be at the Roosevelt Hotel and arrangements are already underway in preparation for this the sixty-ninth meeting of the organization.

BLOOD BANK PROGRAM

The blood bank plan of the American Red Cross was discussed and the Executive Committee went on record as opposing this project as now planned and the national and state Red Cross headquarters and component societies of the State Society have been so informed.

VETERANS ADMINISTRATION CONTRACT

In view of existence of discrepancies and misunderstandings in connection with the contract between the State Society and the Veterans Administration for medical service to veterans, the Executive Committee was of the opinion that the contract should be discontinued. The Veterans Administration, United States senators and representatives from Louisiana and members of the State Society have therefore been informed that the contract is canceled effective June 30, 1948. As stated in the communication to members of the Society this decision was reached after serious consideration and was based on the fact that it is felt that the veteran has not been receiving the benefits of the home treatment plan as was anticipated by the terms of the contract and to continue such a contract would be unfair to the veteran. Members may, of course, continue to treat any present case until discharged but should discontinue taking new cases under the terms of the contract. Termination of the contract between the State Society and the Veterans Administration should in no way prevent members from handling veteran cases on a personal arrangement.

LOUISIANA PHYSICIANS SERVICE

The Executive Committee was of the opinion that a meeting of the Liaison Committee of the Louisiana Physicians Service and the Executive Committee of the Hospital Service Association of New Orleans should be held as soon as possible and the Secretary was instructed to communicate with the Hospital Service Association to this effect.

LEGISLATIVE BILLS

The Committee on Public Policy and Legislation has been actively engaged in studying and opposing or sponsoring bills presented before the state legislature and a full report of this activity will be published for the benefit of members of the Society in a future issue of the Journal. This committee, of which Dr. Roy B. Harrison is chairman, has spent considerable time in Baton Rouge and it is through their effort and effort of other members who have assisted them, that undesirable legislation has been defeated and bills for constructive medical projects have been favorably acted upon. Our individual members should be cognizant and appreciative of this active, alert group of doctors who have done so much for organized medicine.

CONGRESSIONAL MATTERS

Action of the United States Senate in approving Senate Resolution 249, during the month of June, has put to rest for a while at least the Murray, Wagner, Dingell Bill and all bills proposing some form of federalization of medicine. Through appropriate committees the situation as to needs, financing and applicability for any improvement in medical care which this country might need, will be studied and report should be made in the Senate during the early part of 1949. Certainly political changes between now and then may influence the future course of this legislation. Action of the Senate in this regard was primarily due to three important factors:

(1) Breaking down of the selective service records of World War II, adversely to proponents of federalized medicine who leaned over backward on the implication that the great number of rejections was due to remedial causes. (2) The Brookings Report—a non-partisan report, prepared at the request of Senator Smith, on the needs of medical care, necessity for government supervision and future benefits, if any, to be derived if such a law is passed. This report was favorable to the cause of organized medicine and had a tremendous influence upon the Senate committee and the public. (3) Opposition of the medical profession.

We must not now, in the face of these achievements, become complacent or too jubilant about the future. It should be remembered that there is a national election and politics and individuals may have a tremendous bearing on the direction our government of the future will take. Be sure to keep vigilant.

MEDICAL CARE FOR VETERANS

Following is information contained in a communication received from the Veterans Administration by the Secretary-Treasurer of the State Society:

> "In the event that the renewal of the contract between the Louisiana State Medical Society and the Veterans Administration is not made by 1st of July, 1948, fees listed in VA Catalog No. 5 will be used, provided they do not exceed rates charged the general public for similar services."

It should be thoroughly understood that in view of the recent cancellation of the contract between the Veterans Administration and the Louisiana State Medical Society any acceptance of such a national fee schedule will be on a personal basis with the Veterans Administration as this is not in accord with the previous contract or intention of the Executive Committee of the State Society for the future. It is hoped that members of the Society will be guided accordingly and will be very alert in determining the nature of this agreement before participating in it.

LOUISIANA STATE MEDICAL SOCIETY NEWS

CALENDAR

PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

A meeting of the Sixth District Medical Society was held at Pallud's, Baton Rouge, on Tuesday, May 25.

The scientific program consisted of a lecture by Dr. Donovan C. Browne, of New Orleans, on results of proctoscopic examinations in a large series of cases. Dr. A. V. Friedrichs, of New Orleans, spoke on the work that the State Medical Society is doing to promote better public relations.

New officers elected were as follows:

President—Dr. H. Guy Riche, Sr., Baton Rouge.
Secretary—Dr. J. DeLoach Thames, Hammond.
Treasurer—Dr. Cecil Lorio, Baton Rouge.

Vice-Presidents: Ascension—Dr. D. C. Brumfield, Darrow; East Feliciana—Dr. E. M. Robards, Jackson; East Baton Rouge—Dr. Charles McVea, Baton Rouge; Iberville—Dr. Eugene Holloway, Plaquemine; Livingston—Dr. M. Williams, Denham Springs; Tangipahoa—Dr. M. B. Small, Kentwood; St. Helena—Dr. C. S. Toler, Clinton;

St. Tammany—Dr. Carl Young, Covington; Washington—Dr. Wm. S. Harrell, Bogalusa; West Baton Rouge—Dr. George Thomas, Port Allen; West Feliciana—Dr. C. J. Wise, Angola; Point Coupee—Dr. F. F. Rougon, New Roads.

The fall meeting of the Society will be held at Cave Tangi, Hammond, sometime in November.

L.S.U. MEDICAL ALUMNI ASSOCIATION

One hundred and thirty-five physicians attended the quarterly meeting of the New Orleans District of the L.S.U. Medical Alumni Association at Arnaud's Restaurant on June 10. Dr. Harold W. Stoke, President of Louisiana State University, spoke on "Progressive Medical Education". During his talk he stressed the need for the proposed $2,000,000 eight-story addition to the present medical school building to provide additional classrooms, office space, a 500-seat auditorium, student laboratories, and research laboratories, which facilities would eventually allow the school to increase its enrollment by 20 per cent. Dr. Vernon Lippard, Dean of the Medical School, and Dr. Tom Richardson of Minden, Louisiana, President of the State Medical Alumni Association, also spoke. Dr. Jack R. Anderson, President of the New Orleans District, presided and announced that the Alumni Association would work for construction of a student dormitory and cafeteria. The next meeting of the L.S.U. Medical Alumni Association will be held in September.

NEWS ITEMS

Dr. Rudolph Matas has been awarded a life membership certificate in the Louisiana State Pharmaceutical Association. This was presented to him by Mr. William P. O'Brien, president of the association on May 5, 1948. It was given in recognition and appreciation of Dr. Matas' life-long friendship and assistance to the Louisiana State Pharmaceutical Association.

Eighty members of the graduating class of the School of Medicine, Louisiana State University, were awarded the M. D. degree at commencement exercises on May 29. The George S. Bel Memorial Award for outstanding scholarship was presented to Nicholas J. Olivier of New Orleans.

Dr. Charles M. Goss, professor of anatomy, School of Medicine, Louisiana State University, has been elected editor-in-chief of the Anatomical Record.

Dr. G. John Buddingh, formerly professor of bacteriology, Vanderbilt University School of Medicine, has been appointed professor of microbiology at the School of Medicine, Louisiana State University, effective July 1. Other recent appointments to the full-time faculty include Dr. Ruth A. Miller, formerly of Johns Hopkins School of Medicine, as assistant professor of anatomy; Dr. William Obrinsky of New York, instructor in pediatrics; Dr. Thomas Hernandez of New Orleans, instructor in biochemistry; Dr. Irving M. Essrig of New Orleans, instructor in surgery; Dr. Jack C. Miller of New Orleans, instructor in obstetrics and gynecology.

Doctor Lucien A. LeDoux, President of the Southern Medical Association, attended a meeting of the Executive Council, which was held in Birmingham, Alabama on May 15. Among the many important matters discussed was one referring to the next convention meeting place and it was decided that the 1948 Meeting will be held in Miami, Florida the latter part of October. The exact dates and the convention headquarters hotel will be announced in the next issue of the Southern Medical Bulletin.

Dr. Julius Davenport, Jr., Southern Baptist Hospital, New Orleans, has been appointed official representative in Louisiana of the American Association of Blood Banks. Any questions relating to this Association should be referred to Dr. Davenport.

PROFESSIONAL OPPORTUNITY

A member of the State Society in Red River Parish is planning to retire shortly and would like to dispose of the facilities in connection with his medical practice. It is his preference that this be taken over by a young doctor since there is opportunity for a very active practice. There is available a two story fifteen bed brick hospital including complete operating room and instruments, delivery room, autoclave, x-ray, and diathermy. Adjacent to the hospital is a five room office building complete with laboratory and with a colored ward in the rear. For further information contact Dr. L. S. Huckabay, Coushatta, or the office of the Journal.

VETERANS ADMINISTRATION MEDICAL RECORDS

The Veterans Administration has in its custody the majority of syphilis records of those Army personnel who were treated for this disease while in active service, and in many instances can procure informative data from the syphilis records of other than Army personnel. It is thought that many physicians treating veterans for syphilis as private patients would find a resume of the syphilis record useful since the details of treatment, results of spinal fluid examinations, and blood serologies are incorporated in the records.

Resumes of these records are available to physicians who are treating such veterans provided authorization for the release of the data is given by the veteran. Requests for the resumes accompanied by an authorization for the release of the data, dated and signed by the veteran, should be addressed to the Dermatology and Syphilology Sec-

tion, Veterans Administration, Munitions Building, Washington 25, D. C. It is most important that the veteran's Service Serial Number and other identifying information, such as the date of enlistment, the date of discharge, rank, and organization be included.

Ordinarily, the resumes can be furnished in approximately two weeks from the date of the receipt of the request and signed authorization.

NAVY'S NEW MEDICAL TRAINING PROGRAM

The Surgeon General of the Navy has announced the expansion of the Bureau's professional training program for reserve and regular medical officers, which is similar to the recently expanded Army medical training program. The object is to permit more Navy doctors to meet the requirements for certification by the various American Specialty boards, and to encourage the young doctor to intern under the auspices of the Navy. The following are the important points in this program:

Graduates of Class A medical schools who have been accepted for internship by a hospital approved for such training by the Council on Medical Education and Hospitals of the A. M. A. may be commissioned as lieutenants (junior grade), MC, USNR, and permitted to continue their intern training. They will receive all the pay and allowance of the rank while so serving. After completing their internships, the medical officers must remain on active duty for a period of one year. If they meet the professional, physical and moral requirements, they will be given every encouragement to transfer to the regular Navy.

Interns who have completed the one year of obligated service, and who have transferred to the regular Navy, may be considered for residency training on a competitive basis with other officer personnel of the regular Medical Corps.

Resident physicians now in civilian hospitals, or those accepted for approved residency training, are eligible for commissions in the regular Navy. Those so commissioned will be assigned to duty, with full pay and allowances, in the hospital in which they are already a resident, or to which they have been accepted for residency training. Every attempt will be made to permit residents holding commissions in the regular Navy to complete their training in event of an emergency.

The obligated service following graduate medical training (courses, fellowships and residencies) in Naval hospitals is one year for each year of training received.

Information concerning any part of the program may be obtained by writing to the Chief of the Bureau of Medicine and Surgery, Navy Department, Washington 25, D. C.

AMERICAN ACADEMY OF GENERAL PRACTICE

Dr. J. P. Sanders, of Shreveport, was recently elected Vice-President of the American Academy of General Practitioners at a meeting held in Chicago.

WOMAN'S AUXILIARY PRESIDENT'S GREETING

As president of the Woman's Auxiliary to the Louisiana State Medical Society I wish to extend greetings and best wishes to all members of the Auxiliary and to my prospective members.

It is a great honor to be chosen president of this organization for which I am deeply grateful and humble. I have endeavored to acquaint myself with the mechanism which activates this Auxiliary. There is still much to be learned and can only be learned by actually doing the things expected of a person assuming this office.

The Auxiliary has had a phenomenal growth under the capable direction of the splendid group of presidents who preceded me. With the cooperation of the entire Auxiliary the new president may hope in a small way to emulate the example of the distinguished past presidents.

The Auxiliary members seem happy about our new publication. We owe a debt of gratitude to the Council on Medical Service and Public Relations of the Louisiana State Medical Society for naming, publishing and mailing our little magazine which was born during the recent state convention held in Monroe. Like all newborns its future is not clearly foreseen but we want it to be a mouthpiece of information and help in the work of the Auxiliary. You can help feed the new baby with ideas, plans and suggestions. In the first issue we hope to have information which will reach you in time for year-book making and planning of general work.

Any worthwhile enterprise must grow and expand its services to its members and to the public at large in order to be alive and alert. This shall be the aim of my term of office.

We invite your help, your ideas and your criticism. We will make every effort to make the best possible use of them.

MRS. O. B. OWENS,
State President

BOOK REVIEWS

Scientists Starred, 1903-43 in "American Men of Science": by Stephen Sargent Visher, Baltimore, John Hopkins Press, 1947. Pp. 556. Price $4.50.

The late J. McKeen Cattell created the directory American Men of Science. In the seven editions since 1906, an asterisk has been placed before the

names of 2,607 scientists. These were chosen by leading research scientists on the basis of their knowledge of the individuals and their scientific attainment.

Dr. Visher has made a detailed study of these starred scientists as to their preliminary, collegiate and doctoral training, place of birth, geographic distribution, background, developmental and other influences. If utility is to be a criterion by which to measure Dr. Visher's work, the result will be disappointing. Many of these scientists were highly trained while others attended institutions not well known and some have had relatively little basic training but "Scientists Starred" is exceedingly interesting and represents a truly great piece of research study even though it resulted in no formula for the mixing of certain ingredients which would ultimately produce great or distinguished scientists.

The author himself concludes that "Large classes and student body are unfavorable to the production of future scientists" and that science students must have intimate contact with stimulating teachers.

H. W. KOSTMAYER, M. D.

Physiology of Man in the Desert, by E. F. Adolph and associates. New York, Interscience Publishers, 1947. Pp. 357. Price, $6.50.

This book presents data collected by a number of observers. The results are well illustrated by numerous charts throughout the book. The methods of investigation were the best available under the circumstances, but numerous problems are left unanswered. It is difficult to obtain an adequate series of controls under the conditions of the experiments.

The greater part of the book deals with water balance and protection from heat. The endurance of man under varying amounts of water deprivation is presented. Methods of protection against the extreme physiologic demands of a hot and dry environment are adequately discussed and illustrated.

More attention might have been given to electrolyte balance. The role of the kidney in maintaining isotonocity, particularly of sodium, seems neglected.

The text could well be condensed by eliminating repetition in the chapters written by the various contributors.

This book presents important data on the normal physiologic reaction of man to life in the desert and is a valuable contribution to the literature on this subject.

THORPE RAY, M. D.

Clinical Toxicology, by Clinton H. Thienes and Thomas J. Haley. Second Edition. Publisher: Lea and Febiger, Philadelphia, 1948. Pp. 373. Price $4.75.

In preparing a textbook on toxicology authors are undoubtedly confronted with the difficulty of dealing adequately with an almost endless list of drugs and chemicals which are potential poisons. This is especially true if the field of organic industrial poisons is included. A work, encyclopedic in nature may be attempted or as an alternative a shorter book probably more suitable for the student or practicing physician may be written by judicious selection of substances for consideration and by avoiding where possible discussion of controversial mechanisms of action and methods of treatment. The present authors have followed the latter course. As stated in the preface the poisons described are those most frequently encountered or those which serve to typify a certain group of poisons. The classification of contents is according to major toxic action rather than by chemical structure. This is indicated by such chapter headings as cerebral convulsants, cord convulsants, toxicology of general anesthetics, muscle poisons, cardiac poisons, local irritants and corrosives, kidney poisons, poisons of mineral origin, bone marrow poisoning, etc. Each poison is discussed where applicable under such headings as toxic dose, etiology, absorption, symptoms and action, duration, fate and excretion, pathology, diagnosis and treatment. A useful section of the book concerns general principles of treatment. This is followed by an outline of symptom diagnosis in which the various drugs are listed which may cause such effects as circulatory collapse, hemorrhage, convulsions, constipation, etc. A section on chemical diagnosis of poisoning is of more interest to the toxocologist than to the general practitioner. It describes some of the more specific chemical tests and a few biological tests. Most of these are qualitative in nature but quantitative procedures for arsenic, bismuth, lead and mercury are included. The value of a synoptic work of this nature in which numerous statements are at least questionable would be increased by a bibliography.

RALPH G. SMITH, M. D.

Private Enterprise or Government in Medicine, by Louis H. Bauer, M. D. Charles C. Thomas, Springfield, 1948. Pp. 201. Price $5.00.

This small volume describes the growth of government in medicine, the development of compulsory sickness insurance, both in this country and abroad, and draws several conclusions regarding health conditions in the United States. It also outlines the program of the American Medical Association, and recently proposed federal health legislation. The theme of the book is that compulsory insurance is un-American and that it encroaches on the freedom of the individual until he has nothing left. The conclusion presented is that group hospitalization and voluntary medical care

insurance of various types will eventually meet the needs of this country and make any compulsory plans unnecessary.

CLAUDIA PYE.

Psychopathology and Education of the Brain-Injured Child, by Alfred A. Strauss and Laura E. Lehtinen. New York, Grune & Stratton, 1947. Pp. 206. Price $5.00.

This scholarly presentation of the brain injured child from a combined neurological, psychological and educational point of view should be of interest to both psychiatrists and pediatricians. It is recommended as required reading for medical students in pediatrics, teachers of special classes, nurses specializing in pediatrics, and graduate students in psychology. The book is a culmination of many previous studies by Dr. Strauss concerning the mental organization of the child with brain injury, his disturbances in perception and thinking, and his deviations in behavior. The contributions of Gestalt psychology to the understanding of such children's difficulties are explained; and the approach to the problem with studies by Goldstein of brain-injured adults is illustrated. Recent clinical-psychologic studies are cited.

Detailed case histories, drawings and diagrams of the brain, and illustrations of tests used make the book both easily read and interesting. Many psychologists have been seeking for tests best suited to children with organic brain damage, and this book is the answer to their quest. References and bibliography are thorough.

The section on education should be recommended particularly to superintendents of schools and directors of special education.

The book fills a real need, is sound in its psychologic approach, and contributes helpful material on a subject concerning which all too little is known by those dealing with brain injured children.

MARION FONT.

PUBLICATIONS RECEIVED

Blakiston Company, Philadelphia: Practical Bacteriology, Hematology, and Parasitology (10th edition), by E. R. Stitt, M. D., Ph. M., Sc. D., LL. D., Paul W. Clough, M. D., and Sara E. Branham, M. D., Ph. D., Sc. D.

Doubleday & Company, Inc., New York: Successful Marriage, edited by Morris Fishbein, M. D. and Ernest W. Burgess, Ph. D.

Froben Press, Inc., New York: Essays on Historical Medicine, by Bernard J. Ficarra, A. B., Sc. B., M. D.

Rodale Press, Emmaus, Pennsylvania: The Healthy Hunzas, by J. I. Rodale.

W. B. Saunders, Philadelphia: A History of the Heart and the Circulation, by Frederick A. Willius, M. D., M. S. in Med. and Thomas J. Dry, M. A., M. D., Ch. B., M. S. in Med.; Modern Clinical Psychiatry (3rd edition), by Arthur P. Noyes, M. D., Treatment of Heart Disease, by William A. Brams, M. S., M. D., Ph. D.

Charles C. Thomas, Springfield, Illinois: Hemostatic Agents, by Walter H. Seegers, M. S., Ph. D. and Elwood A. Sharp, M. D., Sc. D.